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TRANSACTIONS & STUDIES

of the

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Volume 15
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Number 1
(April 1947)

The Diagnosis and Treatment of the Macrocytic Anemias*†

By GEORGE R. MINOT, M.D.

IT IS an honor to be asked to give the Nathan Lewis Hatfield Lecture. I have chosen to speak to you on the macrocytic anemias.

A macrocytic anemia may be defined as one in which there is an increase in the number of red blood cells having a diameter greater than 7.5 (±0.3) microns and a mean corpuscular volume exceeding 95 cubic microns. The color index is usually 1 or more.

Macrocytes come from large bone marrow parents yet we do not know why they arise. Excess of iron pigment may permit red blood cells to become larger. This has been shown by Miller and Rhoads. When they injected in animals blood removed daily, the marrow became erythroblastic and highly cellular. It has been suggested that large red cells with more hemoglobin than normal are an attempt to compensate for a decreased number. There may be large cells with much hemoglobin but a striking deficiency of cells in the blood.

Slight macrocytosis is often present. Distinctive macrocytosis occurs in pernicious anemia and may be found in other conditions than anemias of nutritional origin. There are essentially only iron and liver (or allied substances such as stomach and yeast) that are effective in the treatment of anemia. Recently folic acid has been heard of. It acts somewhat like liver extract and I will comment upon it later on. Nobody knows as yet what the relationship is of folic acid, its conjugates and inhibitors to liver extract.

Treatment with liver depends on the patient's sincere willingness to take by mouth liver, liver extract or the like daily or liver extract intramuscularly every one to three weeks.

Various groups of macrocytic anemias, such as those of aplastic anemia, do not respond to liver, but pernicious anemia, sprue and macrocytic anemia associated with dietary deficiency do respond to liver.

Pernicious Anemia

Thomas Addison, who lived 1793 to 1860, and who was Senior Physician to Guys Hospital, London, first clearly described pernicious anemia at a meeting of the South London Medical Society on Thursday, March 15, 1849

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† Nathan Lewis Hatfield Lecture XXXI, The College of Physicians of Philadelphia. Delivered 5 February 1947, on the occasion of Dr. Minot's induction to Honorary Fellowship in the College.

(1). He wrote, "For a long period I had from time to time met with a very remarkable form of general anemia occurring without any discoverable cause whatever." He thus used the term idiopathic. He said what is essentially true today, "It occurs in both sexes, generally, but not exclusively, beyond the middle period of life, chiefly in persons of a somewhat large and bulky frame and with a strongly marked tendency to the formation of fat."

Castle's dramatic work is well known (2) (3). He has shown that an extrinsic factor in food, such as beef, certain vegetables and so forth, and an intrinsic factor interact essentially to create liver extract. In pernicious anemia there is failure to secrete the unidentified intrinsic factor which is the crucial fault in this disease. Pernicious anemia occurs particularly in the temperate zone and in the white race. It is rare before the age of forty and usually occurs in persons with light-colored eyes and prematurely gray hair. There may be a familial incidence.

Gall bladder dysfunction in pernicious anemia is common. The onset of the disease is insidious. Soreness of the tongue may occur early. Clinically the spleen used to be often palpable but it is rarely felt today because patients are kept well with liver. Suitable amounts of liver prevent the development of nervous lesions and their symptoms. Subjective sensory disturbances are the most frequent evidence of involvement of the nervous system. Diffuse, uneven degeneration of particularly the posterior and lateral tracts of the spinal cord and degeneration of the peripheral nerves are common. Liver therapy causes the peripheral nerves to regenerate but it cannot regenerate the damaged spinal cord. Diminution or loss of vibratory sense is common. This develops usually bilaterally and especially in the lower extremities. Lack of smell and loss of taste, especially for protein foods, occurs. Occasionally the nerve lesions occur long before there is any anemia. Why there are more cord lesions in pernicious anemia than in sprue is unknown. Patients with spinal cord lesions must not stay in bed but must start walking very soon. The tuning fork should be used in suspicious cases as it readily determines if there is abnormality of the vibration sense. Spontaneous remissions, a feature of the disease before the days of liver therapy, essentially do not occur today.

The abnormality of hemopoiesis is inhibition of cell capacity for division. The macrocytosis is marked and the cells tend to be oval, more markedly so than in other anemias. The more the anemia, the more marked are the changes in the sizes and shapes of the red cells and the red count is often found to be lower than the patient suggests.

Daland, Heath and I (4) have studied the red cell size and shape in pernicious anemia, refractory and other macrocytic anemias. Below the level of about 2,500,000 red blood cells per cu. mm. the degree of anisocytosis revealed by the standard deviation and the coefficient of variation of the red cell diameters serves as a fairly accurate criterion for distinguishing pernicious anemia from many other types of macrocytic anemia. The standard deviation measures the spread of the varying sizes of red blood cells.

Below the level of 3,000,000 red blood cells per cu. mm. the asymmetric skewness of the distribution curve of the red blood cell diameter in pernicious anemia is an aid in distinguishing these cases from certain other types of macrocytic anemia.

Eosinophilia occurs after raw or cooked liver is taken and the eosinophiles may reach a very high percentage. Before liver was used even 15 to 20 per cent of eosinophiles were occasionally observed. The platelets are reduced. In a broad sense, the fewer the platelets, the sicker the patient. Serum iron is increased because of red blood cell destruction but it rapidly falls on the administration of liver extract.

Gastric achlorhydria often precedes the anemia by many years. The presence of gastric hydrochloric acid makes the diagnosis of pernicious anemia very doubtful. About 40 per cent of cases are diagnosed within a

year. Diagnostic difficulty may occur in the presence of severe infections or other diseases that may inhibit the response to liver extract but this is rare. Nerve symptoms with a normal blood and patients who have been treated inadequately may confuse the diagnosis.

Treatment consists of giving liver daily or an appropriate substitute intramuscularly approximately every one to three weeks. Large amounts must be given to patients with nerve lesions. Liver extract is 60 to 100 times as effective hypodermically as by mouth. The patient should have at least the equivalent of a unit a day. A very large dose of liver extract perhaps may not give as good a result as a moderate amount. This may be because of the adverse effect of biotin, which is present in generous amounts in some preparations such as Liver Extract 343 (Lilly). L. S. P. Davidson and associates (5) have shown that within 6 hours after liver extract is given intramuscularly megaloblasts disappear from the marrow. Dr. C. S. Davidson and associates (6) of my clinic, have shown that multiple transfusions of blood also may cause rapid disappearance of the marrow megaloblasts but they cause no increase in white blood cells or blood platelets or increased sense of well being except as due to the increased amount of blood. Whole liver in contrast to liver extract perhaps has some unknown beneficial effect for patients with central nervous system lesions. Such treatment for peripheral neuritis is also wise perhaps because it will supply large amounts of Vitamin B.

Today one need not die of pernicious anemia and the treatment does seem to be simple.

Sprue

The name sprue was suggested by Sir Patrick Manson in 1880. The condition simulates pernicious anemia. Idiopathic steatorrhea found in non-tropical countries and celiac disease, especially in children up to the age of two, are essentially the same. Sprue is a wasting disorder. Glossitis is prominent, and diarrhea with bulky, frothy stools is a feature. Chronic indigestion for some months is a common mode of onset. In pernicious anemia there may be severe glossitis and diarrhea and one may not be able to tell whether the patient has pernicious anemia or sprue (7). In early sprue there is a strawberry-colored appearance of the tongue. Often there is intolerance to carbohydrate and fat and usually abdominal discomfort appears following the ingestion of food. The colon is often dilated and there may be only one bulky, pale stool a day. Nervous instability, mental depression and asthenia are common. Areas of brownish pigmentation with roughening of the skin may be found. Cord lesions do not occur. Macrocytic anemia may be severe and closely resemble the anemia of pernicious anemia. There are many enlarged, oval red blood cells and the mean corpuscular volume may be 150 cubic microns in contrast to a normal of not over 95 cubic microns. Rarely there is a microcytic, hypochromic type of anemia.

Free hydrochloric acid is more often present than absent in the gastric contents.

Probably sprue responds more slowly to diet and liver therapy than pernicious anemia. The diet should be low in fat and carbohydrate but high in protein. Liver soup was used by the natives of Ceylon for centuries. Liver therapy usually checks the severe diarrhea and skim milk, meat and bananas to the exclusion of other foods also do so. After the patient is entirely well, liver therapy does not need to be continued as it does in pernicious anemia.

Aplastic Anemia

Aplastic anemia is a progressive anemia essentially without regeneration. It may be caused by benzol and the like though its cause is often unknown (8). Nerve lesions are not present. The anemia may be macrocytic but often the red corpuscles are approximately normal. The leucocyte count and blood platelets are usually low. Remissions are very rare but increasing degrees of macrocytosis may indicate their onset. There is an absence of glossitis and achlorhydria is not common. One must always consider the possible exposure to

any substance containing the benzene ring and exposure to such hemotoxic drugs must be prevented.

The patients must be given a good diet and transfusions of blood may help. Splenectomy accomplishes nothing. Liver extract may be given a therapeutic trial but no benefit occurs except with rarity.

Macrocytic Nutritional Anemia

Faulty diets of various sorts can lead to anemia. The anemia is often hypochromic and normocytic but macrocytic anemia can occur (9). An occasional case is due to the lack of Wills factor (10). Alcohol addicts frequently have a nutritional macrocytic anemia. The macrocytosis is never as profound as in pernicious anemia and great variation in the shape of the cells does not occur.

Patients with very bad diets may particularly lack Wills factor which occurs in very crude liver extract; that is, cruder than Liver Extract 343 (Lilly). Crude liver extracts given orally have produced complete remissions in Wills factor deficiency, after folic acid has been only partially effective. In such cases purified liver extract effective in pernicious anemia did not relieve the anemia. Macrocytosis is not ever as striking as in pernicious anemia. Glossitis except slight in degree is uncommon and gastric hydrochloric acid is usually present.

Nutritional anemia can be cured by an adequate, well-balanced diet with an ample supply of protein. Liver may hasten the patient's improvement. These patients may respond to a usual dose of refined liver extract given intramuscularly or to oral liver extracts. Sometimes, as with Wills factor deficiency, response will occur only to crude liver extract given orally or to very large amounts given intravenously (11), probably because the Wills factor is contained in the liver extract in very small amounts. The patients may have sparse blood platelets and purpura. In such cases remarkable improvement may occur in a month with oral extract effective in pernicious anemia. Edema occurring during remissions is probably due to protein deficiency because of the rapid utilization of protein in the body by the regenerating blood. The edema soon disappears. Brown hair may fall out and a new growth of white hair occur. Patients with severe nutritional anemia often have peripheral neuritis.

Many of these dietary cases have hydrochloric acid in the stomach, atrophy of the tongue is rare and icterus is lacking. Their maintenance with liver is not required.

Folic acid causes a positive response of the blood in some, but not in all, cases of nutritional macrocytic anemia.

Macrocytic Anemia of Liver Disease and Other Conditions

Macrocytosis is common with liver disease (12). The degree of anemia is seldom profound. The macrocytic anemia is thought to be due to the failure of the liver to act as a storage depot. The blood picture simulates that of nutritional macrocytic anemia rather that that of typical pernicious anemia.

Macrocytic anemia of pregnancy is a rare disorder (13). It is probably a variety of nutritional deficiency anemia. The cases are said to do better with whole liver than liver extract but liver is not needed three months after the baby is born.

The decrease of thyroid excretion causes inhibition of cell maturation so that in severe cases of myxedema a macrocytic anemia develops which is not affected by liver (14).

Pellagra is caused by nutritional deficiency and anemia is not an outstanding feature (15). No liver is needed when the rare macrocytic anemia of this disease is cured.

There are other rare cases of macrocytic anemia of a mild degree and I will mention only that due to infestation of fish tapeworm. The worm inhibits the action of the intrinsic factor of the stomach. Liver therapy, however, relieves the anemia even when the worm has not been expelled (16) (17).

Liver Extract Sensitivity

Individuals may be sensitive to liver extract (18). They suffer from itching of the palms,

have slight flushing and urticaria. Weakness and attacks of asthma, edema of the face and tongue and the like may occur. The patient may become unconscious with a fever reaction. Allergic reactions are more common when liver is given intramuscularly than by mouth (19).

Sensitivity is favored by injection of liver extract over 3 weeks apart. Reactions may occur after liver extract has been well tolerated for weeks or even years, especially after long intervals between injections. There may be both organ sensitivity and species sensitivity. Spontaneous loss of sensitivity occasionally occurs.

Changing the type or source of liver extract may be effective. Cases sensitive to pork liver extract may not be sensitive to beef liver. Sometimes reducing the intramuscular dose to once a week, or desensitization by repeated small injections which are gradually increased is effective. The utilization of a histamine-protein complex as an antigen to produce histamine antibodies also may be distinctly serviceable. Folic acid may be useful to those patients distinctly sensitive to liver for it is said that sensitivity to folic acid will not develop.

Folic Acid

In 1941 Mitchell, Snell and Williams (20), obtained a highly concentrated growth factor for streptococcus lactis R. from spinach and they suggested the name folic acid. In October, 1945, its crystalline synthesis was reported in Science and heralded as a new scientific triumph. The loss of folic acid in cooking is exceedingly high. It is supplied in crystalline form as a bright yellow powder and is used in solution. It is derived from spinach, liver, cereals and other natural sources and is essentially the same as factors promoting the growth of lactobacillus casei (pteroylglutamic acid). Folic acid has essentially the same effect as liver extract on the blood of pernicious anemia and allied conditions (21), but it does not affect any condition that liver extract does not affect. It is not the active principle of liver or stomach, nor is it the extrinsic food factor.

The appetite of the patient with pernicious anemia, sprue and the like rapidly increases; there is disappearance of diarrhea; there is rapid cessation of burning of the tongue and mouth. Folic acid produces results even in the presence of infection. The reticulocyte response to folic acid is perhaps less marked than to liver extract. Folic acid produces the same effect orally as by injection. Cases respond satisfactorily to 10 to 20 mgm. a day but 6 mgm. is too small a dose although even 2 mgm. a day has been effective. Doses as large as 400 mgm. have had no bad effects. Folic acid must be given daily; one third to one half of the dose is lost in the urine in 24 hours (22).

There is evidence that in doses of 15 to 50 mgm. a day, and presumably in much larger doses, folic acid may fail to prevent the development of central nervous system changes. This is a serious drawback to the use of folic acid as well as the fact that it must be taken essentially daily. No reaction to repeated doses of folic acid seems to occur. Patients who have become sensitized to commercial liver extract and who have had extreme local reactions have had no reaction to repeated 20 mgm. of folic acid given intravenously.

There are various sorts of macrocytic anemia which are not aided by liver, such as aplastic anemia. But, whatever the cause may be of a distinctive macrocytic anemia, 150 grams or more of liver taken daily or an appropriate amount of an effective extract is usually effective.

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Present Day Treatment of Arthritis*

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THE TREATMENT of chronic arthritis would probably be considerably simplified if we possessed more concise knowledge concerning the etiology of the disease. As a matter of fact, chronic arthritis shows itself in a number of forms which differ considerably, both in their pathology and in their clinical manifestations. It is, therefore, safe to assume that chronic arthritis is not a single disease entity and that its etiology varies with the clinical picture.

There is much difference of opinion regarding the classification of chronic arthritis. The one now generally accepted is that recommended by both the American Rheumatism Association and the New York Rheumatism Association:

(1) Infectional Arthritis
  a. Of Proved Etiology, microorganism to be specified
(2) Probably Infectional—Etiology Unproved
  a. Arthritis of Rheumatic Fever
  b. Rheumatoid Arthritis
    1. Adult Type
    2. Juvenile Type (Still's Disease)
    3. Ankylosing Spondylitis (Marie-Strümpell)
    4. Psoriatic Arthritis.
(3) Degenerative Arthritis (Hypertrophic Arthritis, Osteoarthritis)
(4) Arthritis Associated with Disturbances of Metabolism
  a. Gout, etc.
(5) Arthritis of Neuropathic Origin
  a. Tabes Dorsalis
(6) Miscellaneous Forms
  a. Arthritis of Serum Sickness
  b. Arthritis of Hemophilia
  c. Pulmonary Osteoarthropathy
  d. Intermittent Hydrarthrosis.

In the present therapeutic discussion I propose to limit my remarks to the treatment of the two most prevalent forms, namely, osteoarthritis and rheumatoid arthritis. These two so-called "great types" of chronic arthritis, including their variants, cover the great bulk of patients which one sees in arthritis clinics and in private practice.

* Delivered at a joint meeting of the College of Physicians of Philadelphia and the Philadelphia County Medical Society, 12 March 1947.

Osteoarthritis

Osteoarthritis is undoubtedly an expression of the aging process as it affects the joints. It is undoubtedly accentuated by excessive wear and tear on the joints. It is often spoken of as degenerative arthritis or degenerative joint disease for the reason that the pathological changes are degenerative rather than inflammatory in character. The interarticular cartilage wears away, the underlying bone becomes condensed and eburnated and often there is cystic degeneration in the underlying bone. The characteristic symptoms of osteoarthritis are pain and stiffness in the affected joint. Swelling is absent unless hydrops develops. The joints most frequently affected are those of the knees, fingers and spine; however, osteoarthritis of the hips is a fairly common condition and, as a matter of fact, osteoarthritis may affect any joint in the body.

The diagnosis is based on the age and occupation of the patient, the physical examination, and the x-ray findings. Radiographs reveal a thinning of the cartilage with hypertrophic and degenerative changes along the articular margins of the adjacent bones. Laboratory studies reveal no characteristic findings. The blood count and urinalysis are usually normal and the blood chemistry shows no specific changes.

The treatment of osteoarthritis is largely symptomatic. Once the destructive changes have taken place in the affected joints, nothing

can be done to restore the joint to its original normal state. However, a great deal can be done to relieve the patient, and in some cases this relief amounts practically to cure. The important thing for the physician to remember is that osteoarthritis can exist sometimes to quite a marked degree without causing any symptoms whatever in the patient.

The successful treatment of osteoarthritis depends upon a correct evaluation of the etiologic factors. Perhaps the most important feature of the treatment is rest for the affected joints. In obese patients, weight reduction is achieved by a low calory diet, supplemented by thyroid extract for those patients whose basal metabolism is below normal. Sodium iodide intravenously once or twice a week has been recommended for this type of arthritis; or hydriodic acid, 1 dram (4cc) three times a day in a half-glass of water can be employed. Physiotherapy and other forms of heat are helpful, but care must be taken in massaging affected joints lest trauma be induced over the hypertrophied margins of bone. Deep x-ray therapy has been recommended by some writers and sometimes gives temporary relief.

Treatment of special forms. The medical treatment of osteoarthritis of the hip is very unsatisfactory. As long as the pain is not too severe, rest, heat, and other conservative measures are all that should be attempted. When the pain and disability are marked, surgery may become necessary. In such cases, arthrodesis gives complete relief, but leaves the patient with a stiff hip joint. Plastic surgery, particularly the vitallium cup operation, is quite popular with some surgeons, but there is some question as to how long the beneficial effect will last.

Painful Heberden's nodes are often relieved by resting the hand as much as possible and by the local use of heat. The paraffin bath is often helpful. The method of applying paraffin is as follows:

Equipment. A candy or fat thermometer.
2–4 pounds of parawax.
1 piece of oil silk, 12″ x 14″.
1 square of absorbent cotton and piece of wool.

Melt parawax over slow fire, then remove from stove and allow it to cool until the thermometer registers 110° to 120°F. Having soaked the hand for about three minutes in hot water, and while still wet, dip in and out of the parawax twelve to fifteen times. Quickly wrap oil silk about parawax which has accumulated on hand, then around that the cotton, and a piece of wool about the whole so that the heat may be retained. Let hand rest quietly in the paraffin pack for about an hour. Then remove the wax, which may be used for the next application.

Rheumatoid Arthritis

The second great type of arthritis is known as rheumatoid or deforming arthritis. This condition may be defined as a chronic systemic disease characterized by inflammatory changes in the synovial membrane and periarticular structures, and by atrophy and rarefaction of the bones. In the earlier stages, the disease manifests itself as a migratory swelling and stiffness of the joints, in the later stages, by more or less deformity and ankylosis.

The etiology of rheumatoid arthritis is not known. For many years it was looked upon as a chronic infection and this point of view is still held by many pathologists. There is a tendency at the present time, however, to place rheumatoid arthritis in the same category with lupus erythematosus, periarteritis nodosa, and scleroderma, and to look upon this whole group as caused by some chronic hypersensitive state of the joint tissue. This hypersensitivity may be due to some microorganism such as the hemolytic streptococcus or it might conceivably be due to some drug or to some product of metabolism. Much interest has been manifested in the close similarity between rheumatic fever and rheumatoid arthritis. The presence in the sera of a high percentage of patients of antibodies against the group A hemolytic streptococcus is one of the striking points in this similarity. The antistreptolysins in the serum of rheumatic fever patients has led to a wide acceptance of the hemolytic streptococcus as the underlying cause of rheumatic fever, though the clinical manifestations in the joints and cardiovascular system are looked upon as an allergic reaction to a streptococcus protein.

In the same way, the presence of the agglutinins against group A hemolytic streptococcus in 60% of patients with rheumatoid arthritis would seem to implicate the hemolytic streptococcus in some way with respect to the etiology of this disease. However, recent studies indicate that the antistreptococcal agglutinins in rheumatoid arthritis may be non-specific in character. The fact remains that there is a considerable group of intermediate cases where the differential diagnosis between subacute rheumatic fever and rheumatoid arthritis is almost impossible to make. This is particularly true in those cases where there are definite clinical and electrocardiographic changes in the heart.

The pathological changes observed in rheumatoid arthritis are not limited to the joints. The marked wasting of the muscles and the atrophy of the skin indicate that the disease is systemic in character, and the recently described collections of small round cells in the muscles and in the paraneuritic tissue go to explain in some measure the muscular and neuritic pains from which so many arthritics suffer. The changes in the joints themselves originate in the synovial membrane where chronic inflammatory changes occur and gradually convert the membrane into a swollen mass of granulation tissue. This process involves the cartilage, with more or less secondary destruction of this tissue, and even the bone eventually becomes affected. The periarticular tissues are also involved in the inflammatory process and this leads to the characteristic swelling.

Symptoms. The onset of rheumatoid arthritis may be marked by no special preceding episode. However, in the majority of cases the patient gives a history of some unusual strain to his physical equilibrium, such as acute infection, exposure to cold, surgical or obstetrical operation, fatigue from overwork, or a long sustained emotional disturbance.

Certain prodromal symptoms are usually noted, the more common of which are weakness and fatigue, loss of weight, anemia, and vasomotor disturbances, particularly tingling and numbness in the hands and feet. The onset may be sudden or gradual. When the onset is acute, the pain and swelling of the joints develop rapidly and are associated with chills, fever, prostration, and other features of an acute illness, but in a great majority of cases the disease makes its appearance insidiously.

When the onset is gradual, symptoms usually appear first in only one joint. Often there is pain and stiffness in this particular joint for weeks or even months before other joints are affected. Gradually the joint begins to swell. The temperature is normal or only slightly elevated, often running for weeks from 99° to 100° F. The pulse is somewhat accelerated, and even early in the disease there may be a secondary hypochromic anemia.

Gradually the disease assumes a chronic course. The characteristic clinical features of rheumatoid arthritis are: swelling of the joints, particularly those of the fingers, hands and knees; the symmetrical distribution of the arthritic manifestations; the migratory character of the joint symptoms, especially in the early stages; the tendency of the disease to progress into a chronic state; and the eventual ankylosis and deformity of the joints if the disease is not arrested.

The degree of pain in the affected joints varies considerably and is not entirely proportional to the amount of swelling in the joint. With many of these patients there is comparatively little pain; in others the pain is excruciating.

As the disease progresses, flexion deformities take place in the elbows and knees, as well as in the fingers and wrists. At first these muscle spasms can be overcome by traction or splints, but as time goes on the joints become fixed in this position and extension becomes more and more difficult. Marked muscular atrophy and wasting leads to still more deformities and subluxations. In the hands, lateral deflection and subluxation at the metacarpophalangeal joints produce the characteristic ulnar deviation which is one of the earmarks of the disease.

On physical examination several of the joints are swollen and tender, most commonly the knees, fingers, and wrists. Later on the elbows, shoulders, ankles, and feet may be implicated. The patients are chronically ill and emotionally depressed. There is usually considerable weight loss and easy fatiguability.

The first attack may terminate spontaneously, to be followed in a few months or maybe a year or two by a second and more persistent attack. Some patients will have several exacerbations and remissions before they finally settle down into the chronic progressive form of the disease.

Laboratory Findings. The positive laboratory findings in rheumatoid arthritis are comparatively few. Radiographs, even after a duration of only six months, will usually show haziness and narrowing of the interarticular space and osteoporosis of the adjacent bones. The interarticular space is thinned more and more as the disease advances until finally it may be completely obliterated.

Secondary macrocytic anemia, sometimes of fairly severe grade, is present in the majority of patients with rheumatoid arthritis. A moderate leukocytosis is found in a considerable number of cases, and the Schilling hemogram frequently shows increase of the immature cells, particularly in active cases.

The sedimentation rate of the red blood cells is increased in approximately 95 per cent of cases. In active cases it may be three or four times the normal rate.

In 70 per cent of well established cases the patient's serum will give a positive agglutination reaction to the hemolytic streptococcus. The albumin-globulin ratio is reversed in the great majority of cases.

The urine shows no characteristic changes.

Treatment. Successful treatment of rheumatoid arthritis depends largely on the promptness and vigor with which it is instituted. It must be admitted at the outset the treatment is purely empirical and not always successful even in the most favorable cases. In a recent article Boots points out that the three methods of treatment which have been most widely publicized in the popular press are all without significant value. They are: (1) massive doses of vitamin D (Ertron); (2) prostigmine; (3) Bogomoletz' Antireticular Cytotoxic Serum. The writer is quite prepared to agree with Boots in expressing marked skepticism concerning the value of any of these forms of therapy.

All authorities are agreed that complete and prolonged rest is the keynote to successful therapy in this disease. This can best be obtained in a hospital or sanitarium, particularly in the earlier stages of treatment. It should be pointed out, however, that patients who receive hospital care, unless febrile, should not be allowed to remain in bed twenty-four hours a day. Such "over-rest" encourages ankylosis of the affected joints and further atrophy of the muscles in the back and legs. In many ambulant cases complete rest is difficult to enforce, chiefly because the patient is eager to keep up his daily duties. However, if these patients in the early stages of rheumatoid arthritis can be persuaded to give up work and take a rest cure for six months or a year, a much higher percentage of them will make a complete and permanent recovery. As it is, and chiefly for economic reasons, the physician must compromise on the rest issue, and the patient is advised to take from one to two hours' rest in bed every day after lunch. If a real rest cure can be taken, it is far preferable, because the patient gets a mental and emotional rest as well as a physical one. In well-established cases rest in bed for a considerable part of the day is absolutely essential. There should also be long sleeping hours at night, induced by some mild hypnotic if necessary.

No special diet is indicated in the treatment of rheumatoid arthritis. Most rheumatoid patients are undernourished and underweight, and one of the duties of the physician is to try to restore the lost weight by means of a nutritious well-balanced diet. In order to achieve this, a high calory, high vitamin diet, rich in vegetables and fruits, is indicated.

Streptococcus vaccine has been employed

for years in the treatment of rheumatoid arthritis and is still popular with some physicians. Vaccines, however, are not used so much now as formerly.

In the writer's opinion, fever therapy has a definite though limited place in the treatment of rheumatoid arthritis. It is not recommended, however, for the chronic well-established cases. In the initial stages of the disease, particularly in acute febrile patients, fever therapy will sometimes bring about a rapid and complete cessation of symptoms. Unfortunately the great majority of these patients who are relieved by fever therapy will suffer a relapse after a few weeks or months of comfort.

There are two methods of inducing fever: (1) typhoid vaccine intravenously; (2) artificial hyperthermia by some form of hot box.

Typhoid vaccine administered intravenously is the simplest and cheapest and, in the writer's opinion, the safest method of employing fever therapy. At the New York Hospital we have used it on many arthritic patients without any untoward effects. It has been found particularly helpful in the active febrile type of case. The first dose should be 25,000,000 bacteria. It is usually desirable to double the dose with each subsequent injection in order to obtain good febrile reactions of 103° to 105° F. The maximum benefit is obtained by the first three or four injections. Typhoid vaccine therapy is contraindicated in patients with chronic cardiac disease, in elderly patients and in individuals who give a history of tuberculosis.

In recent years the artificial production of fever in patients by the use of electricity or the hot box has come into vogue for the treatment of various conditions, and some writers have advocated its use in the treatment of rheumatoid arthritis. Artificial fever is produced by several methods: (1) the hot bath, (2) high frequency diathermy currents, (3) radiothermy, (4) electrically heated cabinets. In the writer's opinion, hyperthermia by induced heat has more disadvantages than typhoid vaccine. The production of heat by radiant energy seems to be the preferable method because of its cheapness, simplicity and freedom from danger. A number of articles have appeared in which it is pointed out that fever therapy as thus produced usually gives only temporary relief. This point of view coincides with the author's experience.

A symptom which frequently needs attention in rheumatoid arthritis is a secondary anemia which usually fails to respond to iron or liver. In such cases a series of blood transfusions will correct the anemia and often start the patient on the road to improvement.

For relief of pain there is no drug that stands up so well as acetylsalicylic acid. The dose should be 10 grains (0.6 Gm.) 3 to 4 times a day, and in some patients even larger doses are well tolerated. There is less danger of gastric disturbance if the drug is combined with sodium bicarbonate or taken with food or a glass of milk.

The one drug which seems to have a definite effect on the course of rheumatoid arthritis is gold in the form of gold salts. Indeed, gold salts are the best medical agent at our disposal for the treatment of rheumatoid arthritis. The forms of gold most popular in arthritis clinics are aurothiomalate of sodium (Myochrysine) and aurothioglucose (Solganol-B).

The dosage of gold salts has been a matter of considerable controversy. In the beginning of gold therapy the dosage varied from 200 to 500 mg. It was soon discovered, however, that such large doses were very dangerous. Freyberg has shown that a dose of even 100 mg. is unnecessarily large and that smaller doses will produce almost equally good clinical results. At the present time the doses which are advocated by most authorities in America are as follows:

First dose—10 mg. intramuscularly.
Second dose—25 mg. intramuscularly.
Third and succeeding doses—50 mg. intramuscularly.

The interval between doses is one week. Some writers advise one repetition each of the small doses before proceeding to the maximum dose. The total amount administered in the course should be 750 to 1000 mg. It is cus-

tomary to administer gold therapy in several series or courses with intervals of four to eight weeks between. The reason for these intervals is to permit the body to excrete some of the accumulated gold.

Unfortunately gold therapy is attended by certain dangers which militate strongly against its wide acceptance. Approximately 25 per cent of the patients on gold therapy develop a rash or some other form of gold intoxication such as stomatitis or gastro-enteritis. Depression of the bone marrow has been observed in a number of cases with a consequent development of hemorrhagic purpura, aplastic anemia or agranulocytosis. A few cases of acute nephritis have followed its use, and there have been rare instances of toxic hepatitis. Because of this tendency toward gold intoxication, which is occasionally fatal, patients who are subjected to gold therapy must be watched carefully for reactions. A blood count and urinalysis should be made at least once a month (oftener in some cases) and the skin carefully observed for drug rashes. In spite of careful supervision, however, an occasional patient will develop an exceedingly unpleasant and persistent exfoliative dermatitis.

Another disappointing feature of gold therapy is the comparatively high percentage of relapses, 50 to 75 per cent in careful follow-ups. Because of this tendency to relapse we have recently been giving our patients maintenance doses of gold salts after the regular course of treatment has been completed. The maintenance dose consists of 25 to 50 mg. of gold salt administered intramuscularly every two to three weeks, and eventually only once a month. We have obtained the impression that the percentage of relapses is considerably reduced by this procedure.

Patients on gold therapy should have determination of the sedimentation rate of the red blood cells about every two to three months. Patients who react well to gold therapy usually have a rapid drop in the sedimentation rate during the first course of treatment. Furthermore, it has been our observation that those who receive marked benefit from gold salts usually show striking improvement from the first course of gold therapy. If a patient shows no improvement after two courses of gold therapy, further administration of the agent is contraindicated.

The more common types of physical therapy, such as dry heat, diathermy, massage and exercises all have a place in the treatment of rheumatoid arthritis. Their chief function is to increase circulation in the affected joints and to preserve as far as possible the tone of the skeletal muscles. Physiotherapy in all forms must be skillfully applied; otherwise it is quite possible to do more harm than good by this method of treatment.

Heat is perhaps the most important form of physical therapy and can be applied either locally to the joint or to the entire body. The local application of heat to one joint is carried out by means of the ordinary electric baker or by diathermy. Some prefer moist heat in the form of hot towels or submersion of the joint in hot water. In the experience of the writer, diathermy is usually disappointing in the treatment of rheumatoid arthritis. From a theoretical standpoint, diathermy should be ideal, as it heats the tissues as well as the skin, but practically, a good many rheumatoid patients, especially those in the active stage, complain that diathermy actually increases the pain. One of the simplest ways of applying heat to the joint is by means of the infrared light. Generalized heat is best applied by means of the hot tub bath, the hot pack or the electric light bridge.

Massage complements heat in that both have more or less the same object, the improvement of blood and lymph flow through the joints. Successful results in the use of massage depend on the qualifications of the masseur and the proper selection of cases for massage therapy. Massage is contraindicated in any patient whose joints are in a highly active, painful stage. However, in many chronic cases there is very little tenderness on pressure over the joints and in such patients massage can be used to great advantage, not only to the joints

themselves, but to the adjacent muscles as well. Massage is of great value in preventing and correcting the contractures that so frequently occur at the knees and elbows.

Exercises. The object of exercises and calisthenics is first to preserve the function of the joint by preventing ankylosis; second, to maintain the tone of the muscles; and third, to prevent and overcome contractions and deformities. Every arthritic should have some exercise, and one of the most important factors in the treatment of arthritis is to determine just the right balance between rest and exercise in the patient's routine. In the average case with several swollen fingers or knuckles and a certain amount of swelling and cartilaginous injury in the knees and feet, ordinary calisthenics taken lying down will usually serve the purpose. The reason for the recumbent posture is to prevent unnecessary strain and fatigue. The arthritic is often unable to understand why he is advised to take calisthenics and yet is forbidden to walk or stand. The reason, of course, is that standing and walking both introduce a certain amount of strain and friction in the joint, whereas when the patient is in a recumbent position all strain on the joint is removed. The tendency of the arthritic joint is to ankylose. The tendency of the arthritic muscle is to undergo atrophy and contraction. Both of these tendencies must be overcome by regular exercises. The writer instructs every patient with arthritis as to the type of exercise suitable for his particular case. The rhythm of the exercise should be slow, as rapid movements may induce stiffness on the following day. Perhaps the most important of the exercises are those that have to do with maintaining posture, and of these the most useful is the quadriceps drill. The patient, lying supine in bed, is instructed to contract and relax the quadriceps muscles 40 to 50 times a day, in order to prevent atrophy and weakness in this important group of muscles. In advanced arthritis, passive exercises may be necessary, or a combination of passive with active exercises. At the New York Hospital we have found active and passive exercises in the warm pool a very valuable procedure in the rehabilitation of the arthritic patient. If a warm pool is not available, the Hubbard-Currence tub provides facilities for exercising the patient under water. The optimum temperature for exercise under water is 98° to 100° F. Higher temperatures are not desirable.

Some rheumatoid patients respond well to a change of climate, particularly when they are transferred to a warm dry climate, such as that of Arizona, New Mexico, Florida, or the West Indies. Holbrook believes that the various forms of heliotherapy constitute the major portion of specific climatotherapy. A physician who advises a patient to take the climate cure should stress the importance of his remaining there for at least six months or even a year. Patients who, for financial or other reasons, cannot make such a pilgrimage should be exposed as much as possible to sunlight and dry heat at home.

If every case of rheumatoid arthritis could receive prompt and efficient medical treatment, comparatively few of them would need orthopedic measures. There are certain simple orthopedic measures with which every physician should be familiar. The arthritic should sleep on a flat bed with only one pillow. Many patients will require a board at the foot of the bed to prevent foot-drop. If the patient shows a tendency to rapid ankylosis, it is important for the physician to be familiar with the optimum position for ankylosed joints, particularly those of the knees, elbows, wrists and fingers. Unfortunately there are a good many individuals who for one reason or another do not receive prompt medical treatment, or perhaps they are lacking in resistance to the disease and advance rapidly to ankylosis and deformity. For such patients, orthopedic procedures of various kinds are of great importance in both prophylaxis and treatment. Some of these measures can be applied to ambulant cases. Others can be used only in institutions. The amount of rehabilitation which may be achieved, even in an advanced case of rheumatoid arthritis, is remarkable, but such improve-

ment requires months or even years of patient care and supervision.

Great strides have been made in recent years in the surgical treatment of arthritic conditions. Manipulation under an anesthetic, synovectomy, arthrodesis, and various reconstruction and arthroplastic operations all have an important place in modern orthopedic surgery. Synovectomy is particularly useful in the correction of rheumatoid knees or elbows which have developed villous arthritis. This operation involves the removal almost en masse of the proliferative synovial membrane. A new synovial membrane may be expected to reform, and a good but not complete range of motion is to be anticipated.

Most patients with rheumatoid arthritis suffer from mental depression and consequently need an abundant measure of psychotherapy. On the other hand, there are some individuals, usually men, who do not take their affliction seriously enough and the physician in all fairness to the patient should make clear to him the serious potentialities of the disease. The small, slender type of neurotic woman is particularly susceptible to rheumatoid arthritis and often responds poorly to treatment. It is this type of patient that needs the greatest amount of moral encouragement. Unless the physician makes very earnest efforts along this line, he will fail to get the full cooperation and confidence of the patient, factors that mean much in the stubborn fight against the disease.

An Evaluation of the Use of Anticoagulant Therapy in Cardio-Vascular Diseases*

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Among the most serious and the most frequent pathological phenomena responsible for disability and death is thrombosis. Thrombosis occurring any place in the vascular tree, either on the arterial or the venous side presents a serious threat to the life of the tissues supplied by or drained by the vessels in which the thrombosis occurs. Each thrombosis of any magnitude also presents a threat to the life of the patient, either by the production of thrombo-embolic phenomena or by the setting up of the phenomenon of serial episodes of thrombosis in various portions of the vascular tree, some of which may be in critical areas and, hence, result in the death of the patient.

The seriousness and the magnitude of this problem for the individual, and for the population as a whole, has never been fully comprehended by the medical profession. It is vitally important that workers devote intense study to the interruption of the mechanism of intra-vascular thrombosis as a pathological condition. It is true that thrombosis is a life-saving mechanism in the cessation or prevention of hemorrhage, but aside from times of war, the number of people who die from thrombosis is far greater than the number who die from hemorrhage. This is especially true in the older age group. During recent years certain materials have been made available which do interfere with the thrombosing mechanism, and may be of therapeutic value when properly used. Chief among these are heparin and dicumarol, and it is the purpose of this paper to present some of the recent advances in the treatment of diseases of heart and blood vessels which are associated with the problem of thrombosis by the use of these substances.

The action of certain impure liver extracts in inhibiting the coagulation of the blood was discovered by McLean, a pupil of Howell in 1916. It required much work before heparin was purified sufficiently to use as an anticoagulant in the treatment of thrombotic conditions such as thrombophlebitis. Heparin is a normal secretion of the mast cells especially in the liver, lung, muscle, intestinal and subcutaneous tissue. Normally, it helps preserve the balance between the clotting and the bleeding tendency of the blood. In the presence of a thrombosing tendency it is necessary to give anticoagulants and heparin may be used for this purpose, since it interferes with the coagulation time and hinders the agglutination and deposition of platelets, thus discouraging thrombus formation. The disadvantages of heparin in the past have been that it has required continuous intravenous infusion, or multiple injections many times a day. Recently, an attempt has been made to use menstrum which permits slow absorption of heparin following intramuscular injection. This has proven to be painful and somewhat difficult to control. When rapid action is necessary, as in the case of an individual who has had numerous pulmonary emboli, heparin is indicated during the first 24-48 hours while the action of dicumarol is beginning to become manifest. Jorpes, Bauer, Crafoord and others have reported excellent results from the use of heparin in thrombophlebitis.

Of recent years, dicumarol has become a widely used anticoagulant. It was first isolated as a result of work carried on to determine the cause of hemorrhagic sweet clover disease in cattle. The first observations in this regard were reported by two veterinarians, Schofield and Roderick. Dicumarol was isolated, identified and synthesized by Link and his co-workers at the University of Wisconsin. These papers were published beginning in 1940. It was demonstrated that the prothrombin level in the blood of animals could be markedly reduced by its administration. In 1941, Meyer, Bingham, and Pohl, Allen and Bollman and Prandoni and Wright presented their findings in Man. All found that in Man as in lower animals, the administration of dicumarol resulted in the prolongation of the prothrombin time and a delay in the coagulation of the blood.

* Summary of presentation before the Section on General Medicine of the College of Physicians of Philadelphia, 25 November 1946.

It was determined that there is a lag of from 24-48 hours before the action on the blood is measurable. They determined that the material was effective when given orally and that fresh transfusions of whole blood would cause a prompt lowering of the prothrombin time if this became necessary. It was also determined that large amounts of Vitamin K would counteract the action of dicumarol when this was indicated.

Since that time large numbers of patients suffering from thrombophlebitis have been treated with this drug. Properly used, it has been found to be the simplest and most effective agent for the reduction of serious complications of thrombosis, including the prevention of thrombo-embolic phenomena available today. In Barker's series of 879 controls who developed thrombophlebitis but who did not receive anticoagulant therapy 95 or 10.6% developed subsequent episodes of thrombophlebitis and 51 or 5.7% died as a result of a fatal pulmonary embolism. In contrast, in a series of 138 similar patients who had thrombophlebitis and who received dicumarol, 4 or 2.9% developed further thrombophlebitis and there were no fatal pulmonary emboli. In 1000 patients given dicumarol post-operatively for the prevention of venous thrombosis, pulmonary embolism and thrombophlebitis of which 379 had already demonstrated a thrombotic tendency in that they had had thrombosis or embolism, and 438 had an abdominal hysterectomy performed (an operation where the statistical risk of thrombosis and embolism is known to be high) there was only one death from pulmonary embolism.

In a control group of 678 patients who had one non-fatal embolism but who did not receive anticoagulant therapy 297 or 43.8% suffered subsequent venous thrombosis, pulmonary embolus or infarction and 124 or 18.3% suffered a subsequent fatal pulmonary embolus. In contrast, of 180 cases who had received dicumarol, only 2 or 1.1% suffered subsequent venous thrombosis, pulmonary embolus or infarction and only 1 or 0.6% suffered a fatal pulmonary embolism, which occurred after the prothrombin time had returned to normal.

The author has had experience with the direct care of more than 400 such cases and the general supervision of approximately an equal number with results paralleling those of Barker. Of these 400 cases 277 were previously non-embolic cases. Three of these developed pulmonary emboli while under anticoagulant therapy. Of 123 patients who had previously suffered one or more pulmonary emboli, two developed emboli while under adequate anticoagulant therapy. There have been no embolic deaths while under anticoagulant therapy. Five patients have continued to have uncontrolled thrombophlebitis. These have had malignancy of the pancreas or liver or phlebitis migrans. Four of these have died of the underlying disease. Hemorrhagic manifestations have been manifested as follows: Purpura, 21 cases, but only two in the last 200; Frank hematuria, 4, but only 2 in the last 200. There have been no deaths in this series from anticoagulant therapy. Bauer, Jorpes, and Zilliacus have reported similar encouraging results from Sweden. Using heparin alone, heparin and dicumarol, and dicumarol alone their figures are about the same. The results with the use of anticoagulant therapy have been better than those following the use of ligation alone—although there may be times when ligation may be wisely used with an anticoagulant, in most instances it is an unnecessary procedure.

Pulmonary emboli have been observed to have originated from the site of ligation and, in numerous instances, to have arisen from sites of thrombosis other than those for which the ligation was done. Anticoagulants tend to seal the thrombus wherever it is located in the entire venous tree.

Beginning in May 1942 we undertook to evaluate the use of dicumarol in the treatment of coronary thrombosis. The war interrupted this work to some degree, but it was possible to continue this study in Army hospitals during the latter years of the war. Recently, we have reported the results in 80 patients with acute or recurrent coronary thrombosis treated with dicumarol. Of these 46 were selected because they were complicated cases having suffered repeated episodes of multiple thrombi of the coronary tree, or embolic phenomena either pulmonary or to other areas. These had arisen from either mural thrombi or thrombi in various segments of the venous tree. 34 of the patients were uncomplicated examples of coronary thrombosis. The results of this series were encouraging. Encouraging results have also been reported by Nichol and Page, and by Peters, Guyther and Brambel—each group having reported 50 cases of coronary thrombosis treated with dicumarol.

The following conclusions seem warranted at this time: (1) In no case was there evidence that dicumarol aggravated or complicated the course of the patient with coronary thrombosis.

(2) It appears physiologically sound to use dicumarol whenever there is a tendency for a thrombus to propagate or multiple thrombi or embolic phenomena to occur. (3) In numerous individual cases it appears that these thrombosing and embolic tendencies are interrupted by the use of dicumarol. (4) The mortality rates for the complicated and uncomplicated cases of coronary thrombosis treated with dicumarol appear to be reduced below the anticipated level for each group, but the total number of patients treated thus far is too small to draw definite conclusions.

A study is being set up now under the auspices of the American Heart Association for a more complete evaluation for the use of anticoagulant therapy in the treatment of coronary thrombosis which should yield valuable and conclusive information within the next several years.

We are also at present studying a group of 12 patients who have had rheumatic heart disease, developed auricular fibrillation, and have suffered from multiple peripheral and pulmonary emboli. Preliminary results with long term ambulatory treatment with dicumarol in these cases is decidedly encouraging and further investigations are being carried out.

Vagotomy and Urecholine in the Treatment of Peptic Ulcer

I. The Treatment of Peptic Ulcer, with Special Reference to Vagotomy*

By JULIAN M. RUFFIN, M.D.

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Introduction

IT IS generally recognized that most patients having a simple, uncomplicated peptic ulcer respond promptly to proper medical treatment and can usually lead a relatively normal existence by careful attention to their diet and daily habits of living. It is true that they will have recurrences from time to time, but for the most part these can be handled effectively by medical measures. However, a fairly large group of patients with peptic ulcer sooner or later come to surgery, and here again gastric resection has proven satisfactory in a large number of cases. Yet, surgery of this type carries a definite mortality and recurrences are all too common. It must be admitted, therefore, that conventional methods of treatment, whether medical or surgical, have failed to afford complete relief in a number of patients. Within the past few years vagotomy has been offered to the profession as a possible solution to the problem which this type of patient presents. The work of Dragstedt (1–5) is familiar to all and need not be reviewed here. The purpose of this communication is to summarize briefly our experience with vagotomy in the treatment of peptic ulcer at Duke Hospital up to the present time, with an impartial evaluation of the procedure giving due emphasis to the complications as well as to the brilliant recoveries which one frequently observers after this type of operation.

Material

In 1944, vagotomy for the treatment of peptic ulcer was introduced at Duke Hospital by Doctor Grimson. Sixty-five patients[1] have had a transthoracic vagotomy for the treatment of their ulcer and constitute the basis of this report. The distribution of cases with duration of symptoms and interval since operation

TABLE I

Transthoracic vagus resection for peptic ulcer

White male	57
White female	4
Colored male	4
Total	65
Duration of symptoms	1–35 years
Average	10 years
Interval since operation	2–29 months
Average	12 months

is shown in Table I. Four patients had a gastric ulcer, nine a marginal, and the remainder had a duodenal lesion. Previous operations had been performed in twenty-four of this group. It should be emphasized that each of these patients had a chronic or recurrent ulcer which had failed to respond satisfactorily to previous medical or surgical treatment. Typical ulcer pain had been present in every case; in fifty-eight this was severe and often intractable. Thirty-three gave a history of repeated massive hemorrhage, and

* This investigation was carried out as a cooperative study in the Departments of Surgery, Biochemistry, Roentgenology, and Medicine by Doctors Keith S. Grimson, Haywood M. Taylor, George J. Baylin, Frederick H. Hesser, and Julian M. Ruffin.

Summary of a paper read before the Section on General Medicine, College of Physicians of Philadelphia, 27 January 1947.

[1] Fifty of these have been reported previously.

the majority were partially or completely disabled because of their ulcer.

Results

The most striking effect of vagotomy is the immediate and complete relief of ulcer pain which was noted in every patient in this series. One patient[2] had a hemorrhage several weeks after vagotomy, but his blood picture was not materially affected and in a follow-up period of over one year he has had no further bleeding. The remaining thirty-two patients with a history of hemorrhage before operation have had no bleeding since. Some patients those patients who had a functioning stoma this was no problem. However, it will be seen from Chart III that nine patients required subsequent gastric surgery because of their retention. Within recent months urecholine has been used successfully in combatting this complication when there was no organic obstruction of the pylorus. This drug was first introduced by Machella (6), who showed that in the motionless, atonic post-vagotomy stomach the administration of urecholine produced large effective peristaltic waves which promptly emptied the stomach. In our experience urecholine by mouth is not effective,

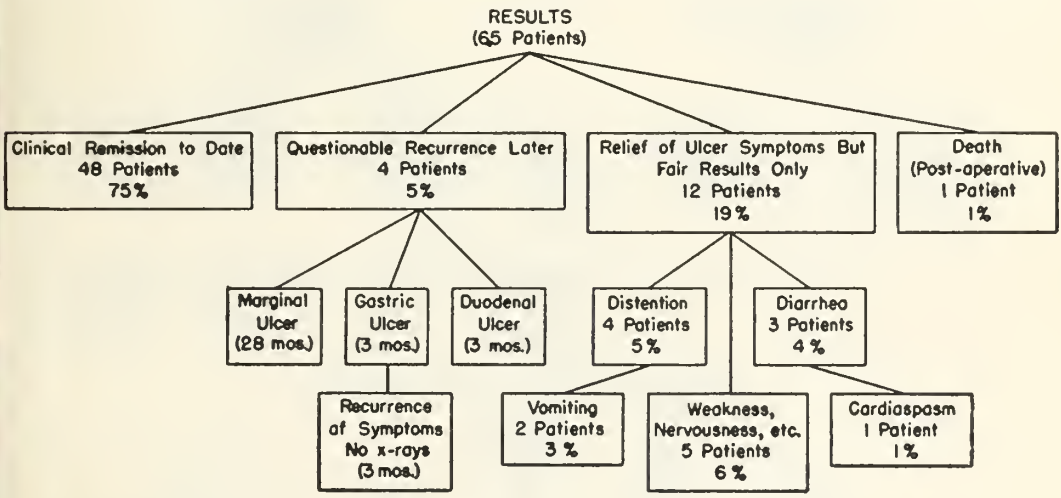


Chart I

obtained fair results only because of distention, diarrhea, vomiting, weakness, nervousness, etc. and there was one post-operative death. Four patients in this series have probably had a recurrence of their ulcer. The results are summarized in Chart I.

Complications

The complications in this group of patients were gastric retention, diarrhea, and cardiospasm (Chart II). By far the most serious of these was gastric retention, which was present in seventy percent of the cases. In probably because of failure of absorption. However, five milligrams intramuscularly results in rapid emptying of the stomach within twenty to thirty minutes.

The second complication of vagotomy has been diarrhea. This occurred in forty-eight percent of the patients as shown in Chart IV. For the most part this was not particularly serious. There was no constant relationship between the diarrhea and achlorhydria (Chart V), nor to gastric retention (Chart VI). An adequate explanation for the diarrhea has yet to be determined.

A third complication was cardiospasm. This occurred in thirty-four percent of the

[2] Reported previously.

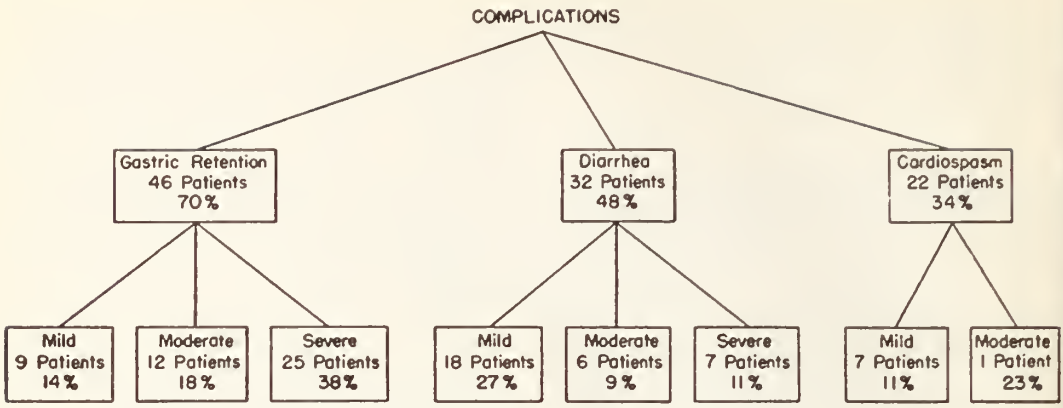


Chart II

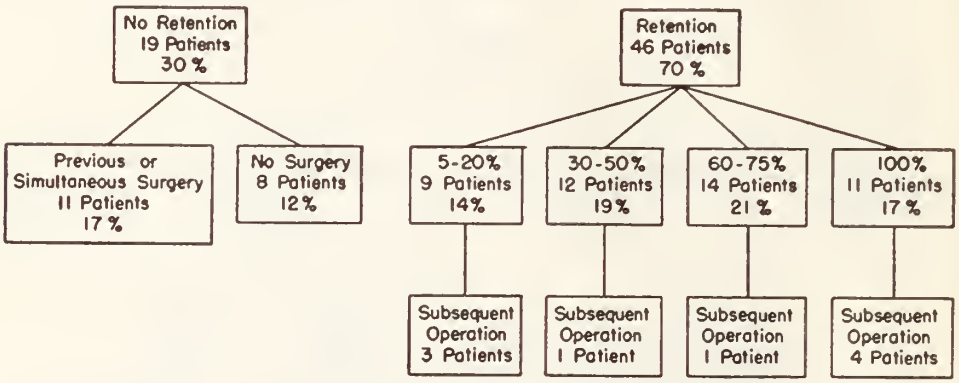


Chart III. Gastric Retention (by X-ray)

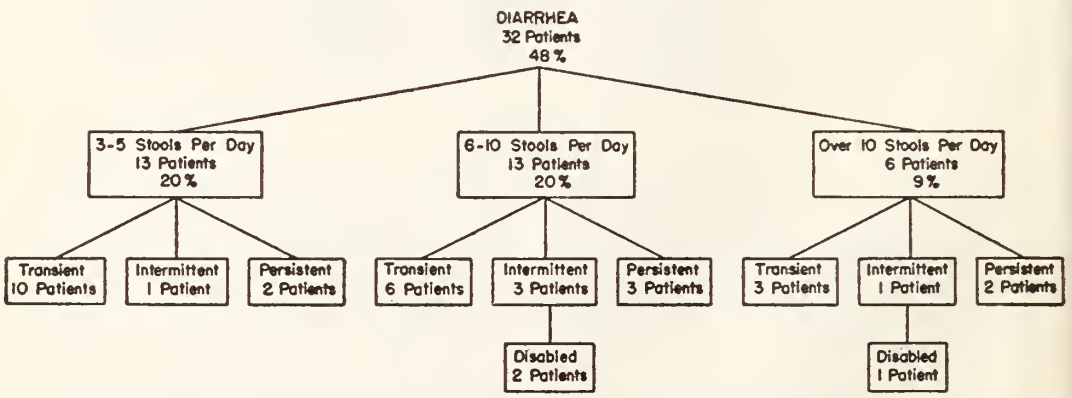


Chart IV

cases, but was usually transient and of no particular significance.

Introduction of HCl into the Stomach

Three hundred cc. of 0.5% HCl were introduced into the stomach by nasal catheter in eleven patients. Six of these patients had a duodenal ulcer, two a gastric, and three a marginal. Each of these eleven patients had a positive "acid test" on several occasions before vagotomy, but after operation the

"acid test" was repeatedly negative in every case.

One patient with a duodenal ulcer, who gave a strongly positive "acid test", was taken to the operating room and anaesthetized in the usual manner, no operation being performed. The "acid test" was repeated as soon as the patient regained consciousness and pain similar to that before anaesthesia was produced. Another patient with a duodenal ulcer was taken to the operating room and after a needle had been introduced for spinal anaesthesia, the "acid test" was performed with the production of severe ulcer pain. Immediately spinal anaesthesia was started with the pain continuing unabated until the anaesthesia had reached the level of the sixth thoracic segment, at which time the pain abruptly disappeared.

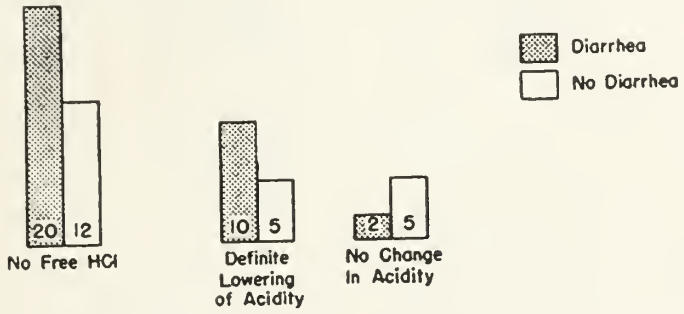
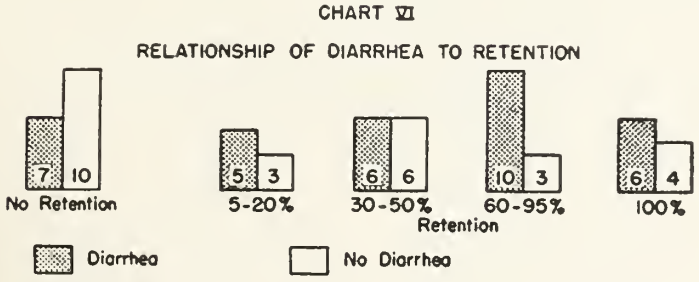


Chart V. Relationship of Diarrhea to Gastric Acidity (Post-operative)



Discussion

It is now well established that transthoracic vagotomy results in dramatic relief of pain in an overwhelming majority of patients having chronic intractable ulcer (7–9). Although a satisfactory explanation for this has not yet been given, evidence at present suggests that it is due to decreased motility rather than to changes in gastric acidity. It is unquestionably true that recurrences have been observed in patients following vagotomy, and it is not yet known whether these were due to an incomplete severing of the vagus nerves or to some other factor as yet undiscovered. The most serious complication of vagotomy is gastric retention and for this reason the procedure should never be performed in a patient who shows any evidence of retention, either clinically or by x-ray. Urecholine is an important drug in combatting this complication. Diarrhea and cardiospasm, while annoying, are less serious and usually require no particular treatment.

Although too short an interval of time has elapsed to fully evaluate the procedure, still it would seem that the brilliant results observed in many cases would justify its use in patients having marginal ulcer following gastric resec-

tion, in patients who have had frequent massive hemorrhages, and in those patients who either fail to recover or are unable to remain well under a carefully planned medical regime. However, it should be recognized that the procedure is still in the experimental stage and should not be performed unless the patient is to be followed carefully over a long period of time. If the results which have been observed to date prove to be lasting, vagotomy may well become the operation of choice in certain patients having intractable peptic ulcer.

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Vagotomy and Urecholine in the Treatment of Peptic Ulcer

II. The Pharmacologic Restoration of Gastric Motility and the Promotion of Evacuation of the Stomach after Section of the Vagus Nerves for Peptic Ulcer*

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ONE of the complications which has followed section of the vagus nerves for peptic ulcer has been gastric retention. This retention has been of sufficient degree to lead to gastric distress, anorexia, nausea, belching, vomiting and loss of weight. It has occurred especially in those patients who have not had a gastroenterostomy or who do not have an adequately functioning one. For the relief of retention, additional surgery, some form of gastroenterostomy, has had to be performed subsequent to the vagotomy.

It has not been possible to determine accurately the incidence of troublesome post-vagotomy retention in the various reports in the literature; it has been estimated to be about 30 percent but may very well be greater. The completeness of the vagisection may be the determining factor.

We have been able to avoid the performance of additional surgery in each of 5 patients by promoting gastric evacuation pharmacologically. For this purpose we have administered the parasympathomimetic drug, urethane of B-methyl choline (Urecholine). An illustrative case will be cited.

Illustrative Case

M. S., a 48 year old private patient of Dr. T. Grier Miller had a transthoracic bilateral vagotomy performed on July 1st by Dr. Julian Johnson. He had had recurrent duodenal ulcer activity over a period of 20 years. Prior to vagotomy, he had an active ulcer demonstrated and there was no roentgenologic evidence of gastric retention. The operation afforded prompt and complete freedom from his ulcer pain. However, shortly after the resumption of oral feedings, he began to complain of anorexia, gastric fullness and nausea. On the 5th postoperative day, he experienced a severe epigastric pain which radiated to his right scapula. Examination of his abdomen revealed that his stomach was distended. Aspiration of the stomach yielded 1300 cc. of gastric content and gave prompt relief from pain. Thereafter, he continued to complain of anorexia, nausea and gastric fullness, and it became necessary to evacuate his stomach at the end of each 24 hours. He lost weight at the rate of a pound per day. On the 16th postoperative day, roentgenologic examination of his stomach revealed it to be in complete and constant diastole. Complete retention of the barium was present at the end of 6 hours. At the end of 24 hours, 50 per cent of the barium was still retained in the stomach. At this time a question was raised as to whether or not gastric surgery might not be necessary for the relief of his retention. Instead, it was found possible to promote satisfactory evacuation by administering Urecholine before or after his main meals. He remained free of symptoms of retention while taking the drug, regained lost weight, resumed his job, and the ulcer healed. After a period of 3 months his stomach began to evacuate spontaneously.

It is next proposed to present roentgenologic and balloon-kymographic evidence of the effects of the drug on the motility of the stomach as well as to describe observations of its effect on gastric acid secretion. These studies were made in conjunction with Drs. Horace Hodges and Stanley Lorber of Dr. Miller's Clinic.

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* Based on a presentation made before the Section on General Medicine, College of Physicians of Philadelphia, 27 January 1947. The subject is more fully treated by the author and his collaborators in *Gastroenterology*, 8: 36–51, Jan., 1947.

A. Effect on Motility and Evacuation of the Post-Vagotomy Retentive Stomach

Roentgenologic evidence.

1. 100 per cent retention of a barium meal 75 minutes after its ingestion was demonstrated.

2. At the end of the 75 minute period of observation, a subcutaneous injection of 10 mg. of Urecholine was given. Eight minutes later powerful peristaltic waves appeared in the antrum; one of them could be seen approaching the pylorus and was associated with the passage of barium into the duodenum.

3. There was practically complete retention of the barium in the stomach of a patient of Drs. Bockus, Hawthorne and Raffenberger at the Graduate Hospital 60 minutes after its ingestion.

4. Five minutes after the injection of the drug, a powerful peristaltic wave was seen approaching the pylorus and barium was seen entering the duodenum.

5. Fifteen minutes after the injection, the stomach was seen largely empty of barium, most of it being in the upper small intestine.

6. Thirty minutes after the injection of the drug, the stomach was seen almost completely empty of barium and the head of the column was in the lower ileum.

Balloon-kymographic evidence.

1. A recording balloon introduced into the antrum of the post-vagotomy retentive stomach revealed an absence of motor activity. However, within 5 to 8 minutes of the injection of a 10 mg. dose of the drug, the level of the tonus rose and powerful contraction waves appeared on the tracing.

2. The period of drug induced activity lasted about 40 to 60 minutes but could be reproduced by a second injection of the drug.

B. Effect on Gastric Acidity

Most drugs of the choline group which stimulate gastric motor activity also stimulate the secretion of hydrochloric acid. Urecholine is no exception. Its ability to increase gastric free acidity naturally gives rise to the question as to whether or not the induced acid secretion might be harmful to the healing of the ulcer. However, as in the case of other choline drugs, the amount of free hydrochloric acid which can be detected after an injection of urecholine depends on whether or not saliva is swallowed:

1. In an experiment in which saliva was not swallowed, there was a moderate increase in free and total acidity in the secretion of the empty stomach following injection of the drug.

2. When the patient was permitted to swallow saliva, there was a slight temporary increase in free acidity. The drug increases salivary secretion; saliva by virtue of its contained mucus can absorb a fair amount of free hydrochloric acid.

3. When the drug was injected simultaneously with the introduction of food into the stomach, no significant amount of free acid was obtained. The neutralizing effect of the food was sufficient to prevent a rise in free acidity.

Thus, the neutralizing effect of the food and of the swallowed saliva can be looked upon as preventing a possible harmful rise in free acidity.

C. Side Effects of the Drug

Parenteral administration.

The subcutaneous injection of the drug in dosage of 10 mg. may be followed by increased salivation, sweating, a feeling of warmth, and, sometimes, by abdominal cramps, a desire to evacuate the bladder and the passage of flatus. As a rule, these side effects are not disturbing to the patient, do not last very long and can be lessened by decreasing the dosage. They are much less severe than those obtained when a similar sized dose of Mecholyl is injected.

Oral administration.

Usually no side effects are noted or complained of.

Practical Points

1. The minimal effective parenteral dose varies from patient to patient and has to be ascertained for the individual. A good starting dose is 5 mgs.

2. The drug is effective when administered orally providing it can find its way into the intestine. Thus far we have not been able to demonstrate sublingual or gastric absorption of the drug. The average patient remains free of symptoms of gastric retention on a 6 to 10 mg. oral dose administered after each meal.

3. The injection of atropine sulfate will abolish the effects of the drug, an intravenous injection more promptly than a subcutaneous one.

4. Some patients will not completely evacuate a 2 glass barium meal after one injection of the drug and may require a second dose; on the other hand in others a single dose of the drug will not only evacuate the stomach completely in 30 minutes, but also carry the head of the barium into the lower ileum. Such rapidity of evacuation and transport is not desirable and can be lessened by decreasing the dose of the drug.

5. The drug is administered before or after each meal until such time as spontaneous gastric evacuation occurs. Spontaneous evacuation of the stomach has occurred in one patient three months post-operatively.

Summary

1. Gastric retention of a distressing nature can occur following bilateral section of the vagi even though there is no retention prior to operation.

2. This gastric retention can be satisfactorily handled by the oral or parenteral administration of Urecholine.

3. The drug can be used over the critical period until spontaneous evacuation occurs, thus eliminating the need for additional surgery for the relief of retention.

4. The drug is not on the market as yet. It is made by Merck and Co. and can be obtained from them for experimental purposes.

5. The action of urecholine in various normal and abnormal conditions, especially postoperative urinary retention have been described by Drs. Starr and Ferguson.*

*Starr, I., and Ferguson, L. K.: Am. J. Med. Sci. 200:372, 1942.

Undesirable Guests and Unwilling Hosts

Parasites in Ancient and Modern Italian Folkmedicine

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A STUDENT of human nature must sometimes wonder whether the worries and dreads of man that are concerned with health or those that spring from monetary matters account for more of his bad hours in life, and whether the art of medicine has not multiplied and aggravated those worries and dreads as knowledge of disease has increased among physicians and been more widely disseminated in popular form and often with commercial intent among their patients. There is no little fascination to be found in the examination of certain conceptions and procedures of medicine as Latin literature of the early Empire reveals them in conjunction with those of such people of Italy today as happen to live out of reach of modern scientific knowledge. In this article we are going to deal with certain physical troubles which would be much less disturbing if we were as devoid of foresight and as free from fastidiousness as are the beasts of the field which are subject to many of the same afflictions, or even, in some cases, if the victim could visualize a little more correctly the interior of his own body.

Parasite is a picturesque word of Greek origin. In the social usage of classical antiquity it brings to mind a humble guest, more or less self-invited to his host's table, earning his meal by playing the role of fun-maker, flatterer, and officious performer of even menial services. He assures himself of a good meal at the side of his patron only so long as he can amuse and blandish his fellow diners acceptably—a precarious calling to follow in the society of either Athens or Rome.

Equally well named is another sort of parasite, one that can never find a friendly disposed host, a parasite that never makes, indeed, any return whatsoever in fun, service, or flattery for the shelter and sustenance that he receives. In fact, a more undesirable and gluttonous guest to provide with food our fancy cannot readily picture. The very names that these parasites bear, Taenia Solium, Oxuris Vermicularis, Flasciola Hepatica, and the rest, however euphonious they sound to our ears, mark them as foreigners, foreigners who justify the worst of xenophobic suspicions and so any alarm that an "America-first" type of citizen could possibly conceive. When, indeed, our physician tells us in plain English that we are playing host to tapeworms, pinworms, flukes, or some other members of the animal world, our first thought is to expel them at once even by the most ignominious route that is available in our body. Fortunately for most of us, we rarely have occasion in the United States to think of any vermicular guest as making a home in us and—still more unpleasant to contemplate—as getting his meals at our expense. All of us do house, to be sure, multitudinous vegetable organisms which we call bacteria, but they are not uniformly bad, and they are so microscopically minute that the Romans lived out their lives in blissful ignorance of their very existence. While, however, they knew nothing of bacteria, they cherished such quaint notions about animals that they knew did live in their bodies or that they mistakenly thought were roving around in them, that these dependents of ours should command some interest. They merit it all the more because some of the notions which the ancients cherished have survived in the folk-beliefs of our own time. There are indeed various physical sensations which readily persuade ignorant people that they are harboring a frog in their throat[1] or a frog,

[1] Notes and Queries, Ser. 6, I (1880), 311.

toad, lizard, or snake in the stomach,[2] one that is only too evidently alive and kicking or squirming.

The treatment which physicians of old inflicted on some of the unwelcome guests of the human body offers certain parallels to the folk medicine of modern Italy with which, I suspect, few classical scholars in our country are familiar. Such survivals in therapy deserve attention, I think, from anybody who is concerned with the history of medicine. We may begin with those parasitical worms which enjoy such melodious scientific names although they exhibit highly obnoxious habits.

Even if we confine ourselves to our Latin references, we have ample evidence that the Roman was often aware of their presence in various parts of his anatomy. The careless and unscientific use of excrements of human and animal origin, not only in agricultural operations[3] but even among the remedies of medicine, could, and still can, account for a considerable population of parasites. People knew little about sanitary principles, little about the transmission of disease. Even now in Italy there are backward communities which live quite unaffected by the teachings of science on these matters. When, however, a Roman did become aware that he had taken on a colonist, his method of expelling it might require as much fortitude in him as the most drastic of those to which his descendants will now resort.

Our earliest Latin reference to a vermifuge is in the *De Agricultura* of Cato, the Censor, whose life of distinction in so many fields covered the eighty-five years from 234 to 149 B. C. Writing on husbandry, as himself a practical farmer, he introduced among his precepts on domestic and rural economy a few very interesting medical recipes. He was a hard man, he worked his slaves nearly to death and then either turned them out or sold them, but self interest required him to keep them fit for their unremitting toil so long as they labored for him. It is easy to imagine the threats to health that one could find on his Sabine farm where human beings lived in unwholesome intimacy with the animals, insect life swarmed, and privy and manure heap were located where they were most accessible with little attention paid to the proximity of larder, kitchen, or the places where the members of the household ate and slept.[4] The ruins of Pompeii afford evidence enough that a stable might adjoin the kitchen and the latter have in it a latrine. And so we find in Cato's manual a prescription for what must have been common enough ailments among his farm people, gripes, diarrhoea, tapeworms, and stomach worms. It requires unripe pomegranates which are to be crushed and put in a jar of strong wine for a month of mingling. Taking a drink of this before eating one's meals would undoubtedly do things to the drinker. The conscientious author of a modern dispensatory when speaking of the use of pomegranate rind as an astringent is likely to add a warning that an overdose can cause visual disturbances, vomiting, purging and a weakness of the lower extremities which may culminate even in paralysis. The bark of the pomegranate root is valued today as a potent taenifuge.

Another of Cato's remedies for worms was to drink *vinum organitum*, that is to say, wine that has been spiced with origan or wild marjoram.[5] For the cure of dyspepsia, worms, and stranguary, he offers recipes that include pomegranate blossoms and fennel. At the end of the prescription we find the quaint direction that the patient shall climb a pillar and jump down ten times, and walk about.

[2] Notes and Queries, Ser. 6, I (1880), 392; Ser. 9. VII (1889), 222–223; 332–333; 390–391; cf. Ser 9, XII (1903). 414–415; Ser 12, III (1917), 490. It is strange to read of live frogs being swallowed for some stomach complaints (e.g., pyrosis, water brash or heartburn) Ser. 1, IV (1857) 145. On the wide currency of the belief: C. S. Burne, *The Handbook of Folklore*, 154.

[3] P. H. Williams, *South Italian Folkways in Europe and America*, 168.

[4] Cat. *De agric.* 126.

[5] Cat. *De Agric.* 127.

A bit of seismic action might encourage the departure of the worms.[5]

The Italian peasant of today knows the pomegranate not only as one of his most beautiful trees in time of fruitage, but also as his benefactor whenever he may have to eject worms from his intestines.[6]

I suppose that the most unpleasant thoughts that can enter one's mind about the tapeworm concern its phenomenal length in conjunction with its somewhat serpentine appearance. But even granting the soundness of a common ancient thesis that the further back in history one goes, the larger are some of Nature's creations, we cannot accept as correct some texts of Pliny that tell us that it can reach a length of three hundred feet. One tenth of that is sufficiently revolting, and is more commensurate with the cubic capacity of its possible lodgings.[7] Neither the ancient nor the modern Italians can be thought of as giants. We must proportion their worms to their stature.

As we should expect, the Latin medical writer Cornelius Celsus had to take note of such a horrible *monstrum*. As a matter of fact, in his treatise *De Medicina* he refers to both the tapeworm and the roundworm, and among the things that he prescribes for their elimination are decoctions of lupines, mulberry bark, pounded hyssop, pepper, scammony, garlic, and pomegranate roots.[8] For the round or thread worms (Oxyuris vermicularis) that particularly trouble children the same remedies were to be used, or some milder ones. Among them he lists preparations of pounded-up seeds of nettles, cabbage or cummin, mint, wormwood, and the seed of cress.[9] Pliny the Elder mentions among the anthelmintics lupines, rue, pepper, ordinary wormwood (Artemisia absinthium) and sea wormwood (Artemisia maritima).[10] We may remark in passing that wormwood was also an ancient agent for keeping down that pest of pests, the clothes moth.[11]

It is interesting to note that in prescribing for children Pliny says[12] that the lupines may be applied externally to the abdomen; for it is in the region of the navel that they are likely to locate their sensation of discomfort. Similarly today the rustic of Perugia will anoint the *ombellico* of the sufferer with hot oil in which he has dissolved the dung of a pig in the hope that at least the worms will resent such nasty treatment from the outside and so decamp.[13]

On the ancient farm, domestic animals, no doubt, showed the same need of being wormed as any of the other laborers. An ox might be more valuable, too, than any ordinary slave. When calves became infested, they would have to swallow balls made of pounded lupines, or a mixture of wormwood with a dry fig and vetch, made up into a similar veterinary pill.

Pig fat mixed with hyssop and juice pressed out of horehound were also thought to be excellent anthelmintics.[14] When the beasts of burden were afflicted with intestinal parasites, they received doses of powdered caper root in vinegar. This, Columella assures us, means death for the worms.[15]

Worms in the ear were another parasitical affliction with which the Romans had to contend. For the removal of such as live near the orifice Celsus recommends the use of an ear-scoop. Martial refers to the use of such an instrument to alleviate the itching, and I had in my collection of Roman antiquities a scoop fashioned out of bone which in moments of vagrant and excited fancy I could claim had served that famous poet. At least no sceptic

[6] C. Coronedi-Berti, "Appunti di medicina popolare bolognese", *Rivista di letteratura popolare* (hereafter abbreviated Appunti) I (1877), 9.

[7] Plin. *N. H.* (hereafter *N. H.* with the numerals) 11.113.

[8] Cels. 4. 24.1.

[9] Cels. 4.24.7; cf. on the *lumbrici* in fever 2, 3, 6.

[10] *N. H.* 22, 155; 27.48; 27.53; 32, 100.

[11] *N. H.* 27, 52. From Cato (*De Agr.* 159) we learn that a rider may prevent chafing by keeping a small branch of Pontic wormwood under his anus.

[12] *N. H.* 22, 155.

[13] Z. Zanetti; *La medicina delle nostre donne* (hereafter abbreviated *La medicina*), 157.

[14] Cels, 6. 25.

[15] Colum. *R. R.* 6.30.9.

had the evidence to disprove it, and politeness forbids any challenging of a "hobbyhorsical" collector by a listener. In order to kill the parasites when they lodged further inside the ear, white hellebore in vinegar was to be used; but for scouring out the dead ones they depended on a decoction of horehound in wine.[16] Wine, we must remember, was the nearest that the ancients could come to modern alcohol. Other prescriptions have come down to us for ridding the ears of worms. One that had urine in it could have made them perhaps uncomfortable.[17]

Many Italians are obsessed by the idea that most of the ills of babies that are not caused by teething are to be attributed to worms.[18] Blondes are reputed to be especially victimized by ascarids. They are said to have a peculiar complexion that indicates their presence, *una carnagione da vermi*.[19] But a light-skinned child is, of course, a rarity among Italians. There is a quaint belief that the two things that are responsible for the existence of worms in the very young are eating cheese and the emotions of terror.[20] And so it is that in the Abruzzi region careful mothers who accept this theory will not take baby in his swaddling-bands before a mirror lest it be terrified, go into a fit, and then get worms. Kissing it on the forehead may also bring them, unless one says *Crisce cappamonde*, an exclamation that is expected to insure a child's growing up in flourishing health.[21]

In order to keep babies from having terrifying nightmares which might be responsible for an infestation by worms, they may be given doses of the brains of a she-goat and wear somewhere on them a piece of the skin of an ass. This is an amulet which has in its favor a long history behind it — let us hope of unqualified success.[22]

According to some Italian wiseacres, you may suspect that an infant's digestive track is infested with a parasite if it keeps rubbing the tip of its nose and sneezes frequently.[23] But there is also a good test of a magical character to which one should resort when baby has convulsions, stomachache, fits of vomiting, or other suspicious symptoms, namely a divination by means of lead, *calibdomanzia*. This has been in use in one form or another for thousands of years in the Mediterranean world. The Italian term for it is *impiombare il bambino*. After the investigator has liquefied the metal on a shovel set over the fire, he drops it into a basin of water which rests on the child's naked belly. If the lead cools into a single drop, there are no worms beneath, but if it forms in the shape of a disc, they are there.[24] While the worst objection that a scientific doctor might make to this would be the fallibility of the diagnosis, an Italian may be wary of it because of his superstitious belief that a child who has been "leaded" will be sure to drown if it ever falls into water that is over its head.[25]

But, as so often happens, magic and religion are made to work together in the maltreatment given parasites. A properly trustful mother will put her baby across her knees and murmur in his ears certain words of incantation. These can be neither taught nor learned except on Christmas night when most people are too busy with other matters to take instruction from the knowing. She then signs him with the sign of the cross. The combination of the charm and the pious gesture should at once start an exodus of all the worms.[26] Some-

[16] Cels, 6.7.5; Mart. 14.23. *Marrubium*, or hoarhound, was a purge: Plin. *N. H.* 20.244.

[17] *N. H.* 28.65.

[18] Z. Zanetti, *La medicina*, 8; *Nonne e bambini* (hereafter abbreviated *Nonne*), 31.

[19] Z. Zanetti; *La medicina* 157.

[20] M. Pasquarelli, "Medicina popolare basilicatese", *Archivio per lo studio delle tradizioni popolari* (hereafter abbreviated *Archivio*), XV (1896), 503.

[21] E. Canziani, "Abruzzese Folklore", *Folklore XXXIX* (1928), 214.

[22] Z. Zanetti, *La medicina*, 154.

[23] Z. Zanetti, *op. cit.*, 155.

[24] Z. Zanetti, *op. cit.* 158. Cf. "casting the heart" for cardiac disease, *op. cit.* 37–38, and for a somewhat different ceremony: M. Placucci, "Usi e pregiudizi dei contadini della Romagna", *Archivio*, III (1884), 527.

[25] Z. Zanetti, *op. cit.*, 158.

[26] Z. Zanetti, *op. cit*, 155; S. Raccuglia, "Medicina popolare siciliana", *Rivista delle tradizioni popolari italiane*, I (1893–1894), 727.

times an Italian who is less tainted by the occultism of the black art merely marks a cross in ink on baby's abdomen in order to accomplish the same result.[27] We must leave undecided whether it is a medical or magical remedy that a woman of Perugia uses when she makes a paste out of a worm that has come from her child and gives it to him in his food or drink in order to rid him of the rest of them.[28]

In the province of Basilicata persons who are troubled by worms put leaves of rue under their pillows to get rid of them by a sort of absent treatment.[29] In Sicily you may hear of a safeguard that is supposed to act continuously against such parasites, namely wearing on the person a cowrie shell (a *conca venerea*) and a tiny male key made of silver.[30] The obscene form of the shell in its resemblance to the pudenda muliebria accounts for its magic efficacy. Of the imperforate key we can speak with less assurance. None of its usual symbolism seems to fit this use.

Among modern "witch-stones", *pietre stregonie*, are various fossil corals which bear the name *pietre stellarie*, because one can see in their structure tiny stars.[31] They enjoy a reputation for preserving their possessor from the fascination of witchcraft and, specifically, from attacks of intestinal parasites.[32] The teeth of sharks in a fossil state go by the name of *lingue di pietra*, "Tongues of stone", or *lingue di S. Paolo*, "Tongues of St. Paul".[33] This shark of a prehistoric age is sometimes identified in the zoology of popular mythology as the *drago* or *granbestia*.[34] In the middle ages such fossils were termed "snake tongues", and like the ammonites (which bear a slight resemblance to a coiled snake) they were thought to cure snake-bites because of their appearance, even as the stone *ophites* had the same reputation back in Roman time as having snake-like markings.[35] The wonder-working *lingue* of Italian superstitition are, doubtless, what the Romans called *glossopetrae*.[36] In Calabria women and children wear them concealed in tiny bags under their shirt, but well-to-do persons may have them in a silver receptacle that is more worthy of their merits. They are given to a baby to help it in its teething (as something on which to bite), save it from intestinal worms, and, of course, in general to protect it against all injuries from an evil eye.[37]

If an uneducated Italian mother has been disillusioned by her experiences with amuletic objects, she may resort to the doctoring of folkmedicine and apply to the nose, temples, and throat of her child certain unguents which the old women of her community recommend as anthelmintic.[38]

Wormwood, Latin *absinthium*, is, of course, Italian *assenzio*. A dose of the tincture does the business well enough in most cases to

[27] P. H. Williams, *South Italian Folkways in Europe and America*, 168.

[28] Z. Zanetti, *La medicina* 156; cf., *Nonne e bambini*, 33; cf. Thomas J. Pettigrew, *On Superstition Connected with the History and Practice of Medicine and Surgery*, 104.

[29] M. Pasquarelli "Medicina popolare basilicatese" (hereafter abbreviated "Medicina"), *Archivio*, XV, 503; cf. G. Di Giovanni, "Usi, costumi, pratiche, credenze e pregiudizi del novarese", *Archivio*, V (1886), 71: rue used to rid children of worms.

[30] G. Pitrè, *Medicina popolare siciliana*, 397.

[31] G. Bellucci, *Il feticismo primitivo in Italia e le sue forme, di adattamento*, 100. P. Saintyves, "Talismans et reliques tombés du ciel", *Revue des études ethnographiques et sociologiques*, II, 182; *Les reliques et les images légendaires*, 207.

[32] Z. Zanetti, *La medicina*, 254; G. Bellucci, *Catalogue descriptif d'une collection d'amulettes italiennes envoyée à l'exposition universelle de Paris*, 1889, tab. VII; cf. G. Palumbo "Credenze e supersitzioni salentine", *Rivista delle tradizioni popolari italiane*, I (1893–1894), 618.

[33] Z. Zanetti, *La medicina*, 254 (*corno di serpente*); 258; G. Bellucci, *Catalogue*, 60, no. 27; P. Saintyves, "Talismans", 183; cf. G. Pitrè, *Medicina*, 298: use of tooth against poison and venomous bites.

[34] R. Corso, "Amuleti contemporanei calabresi", *Revue des études ethnographiques et sociologiques*, II. (1909), 251; G. Calvia, "Essere meravigliosi e fantastici nelle credenze sarde e specialmente di Lagudoro", *Archivio*, XXII (1903), 6 and note 3: "Lamia's tooth", *il dente di Lamia*.

[35] *N. H.* 36. 56.

[36] *N. H.* 37. 164.

[37] G. Bellucci, *Catalogue*, 60, No. 27.

[38] Z. Zanetti, *La medicina*, 156 and note 1.

continue it in favor from century to century.[39] But here again there is danger in taking large amounts of the curative. As a narcotic poison wormwood can cause hallucinations and convulsions—possibly, for all we know, in the thirty-foot worm but certainly in the person who is being wormed. In passing we may note that for worms in the ear drops of juice pressed from leaves of wormwood or from onions is a folk prescription of Perugia.[40]

The juice of garlic is another vermifuge the use of which is doubtless a popular tradition from Roman times. In fact, in addition to an anthelmintic amulet which consists of the vertebrae of a snake that has been bared of its flesh by ants, baby may wear around his neck a necklace of that powerfully prophylactic vegetable.[41] The garlic may not chase away the worms, but it makes it easier, we presume, to find the wearer in the dark. Garlic is also pounded up with mint and moistened with vinegar to make a worm-expelling plaster.[42] The latter, the reader will recall, was one of the ancient vermifuges. The mere odor of garlic (which should be gathered before sunrise on St. John's Day, if it is to possess its full magic virtue) is said to make worms leave their feeding-grounds, although these, according to rustic doctrine, extend all the way from mouth to anus.[43]

Rue has figured almost as a panacea in the pharmacology of twenty centuries.[44] The high value that the Romans set upon it is attested by the story that one of their consuls once made a dole to the populace of honied wine, which had been flavored with it, as an ingratiating gift.[45] We may query whether it would win many votes today even in a liquor drought. The herb was supposed to rid one of worms when it was taken internally[46] or even if it was merely placed on the victim's belly, on the soles of his feet,[47] or, believe it or not, under his pillow.[48] Even the odor of this herb or that of mint is credited with being an expellant.[49]

Actually, medical science teaches us that Ruta graveolens can be a dangerous remedy: locally applied, it is an irritant and vesicant, taken internally, it has caused death by poisoning. An Italian accustomed to rustic doctoring knows how to pound it up with garlic, salt it tastefully, and after mixing a little oil or vinegar with it, put it in a hole made in a child's piece of bread so that he will devour it with a minimum of ruefulness.[50]

But in Italy there are other worms besides the common parasites of the intestinal tract to trouble the imagination and the body. According to vulgar superstition, there is the *fistola*, a small ill-smelling worm which lives in the nostrils, in the lachrymal duct, in the anus, and in the bones.[51] If not fully extracted from its hiding-place, the smallest part of it can regenerate the whole. It causes, you are told, fetid discharges, obstinate suppurations, annoying lachrymation.[52]

Again, in various parts of Italy you will be assured that it is a worm, a *tignola*, that causes toothache by gnawing its way down until it reaches the nerve. Only then may you be aware of its presence.[53] The proper procedure

[39] Z. Zanetti, *Nonne*, 33; C. Coronedi-Berti, *Appunti*, 8; M. Pasquarelli, *Medicina*, XV, 503.

[40] Z. Zanetti, *La medicina*, 187. For onions cf. C. Coronedi-Berti, *Appunti*, 9.

[41] Z. Zanetti, *op. cit.*, 157; *Nonne*, 33; M. Pasquarelli, *op. cit.*, 503; G. Ferraro, "Botanica popolare di Carpeneto D'Acqui", Archivio, IV (1885), 133 (hereafter abbreviated Botanica).

[42] M. Pasquarelli, *loc. cit.* (see note 41). On mint: *op. cit.*, 328.

[43] Z. Zanetti, *La medicina*, 155: C. Coronedi-Berti, *Appunti*, 9.

[44] A. Mancarella, "Superstizioni popolari pugliesi", *Il Folklore Italiano*, V (1930), 145: V. Giangregorio, "Tradizioni popolari di Apice", *Il folklore italiano*, XII (1937), 48: La ruta ogni male stuta. For its wide use in folkmedicine cf. G. Ferraro, *Botanica*, 414; A. D'Amato", Folklore irpino", *Il folklore italiano*, I (1925), 83.

[45] *N. H.* 19. 156.

[46] G. Pinoli, "Medicina popolare nel canavese", Archivio, IV (1885), 79–80.

[47] Z. Zanetti, *La medicina*, 155.

[48] M. Pasquarelli, *Medicina*, XV, 503.

[49] G. Pitrè, *Medicina*, 388.

[50] C. Coronedi-Berti, *Appunti*, 8–9.

[51] Z. Zanetti, *La Medicina*, 177–178; 197.

[52] Z. Zanetti, *op. cit.*, 9; cf G. Pitrè, *Medicina*, 280.

[53] G. Pitrè, *op. cit.*, 334; Z. Zanetti, *La medicina* 8; 179; M. Pasquarelli, *Medicina*, XV, 501: *vermicciattolo*.

is to stop up the hole neatly with a piece of the kernel of a peachstone that has been roasted on a shovel heated red hot, or with ashes left after burning a bone of a toad's leg, or with a piece of gum from the olive tree. Then the creature dies.[54] Anybody who has gazed with relief upon a tooth that has been extracted and seen the pulp extruded from its apices apparently wriggle back into the pulp cavity can readily understand how these beliefs about the *tignola* could have arisen. According to another recipe, the sufferer is to breathe into his open mouth steam rising from boiling water which contains onion seed, and the minute worms will file out of the cavity and drop in the pan.[55] The so-called *erba di S. Apollonia* will rid the sufferer from a whole mess of dental worms. It would appear then, that Apollo, in one form or another, still helps.[56] Saints' names often bear suggestive resemblances to those of the supposedly defunct deities of paganism.

Worms that are too small to be seen by the naked eye are blamed for deep-seated otitis.[57] Moreover, according to what some imaginative Italians will tell you, it is moth-worms that cause blepharitis: the creatures eat the hairs as they would threads of a woolen garment.[58] So when you say humorously that somebody looks a bit moth-eaten about the eyes, you may find an Italian taking you seriously. If you wish to see what these worms look like, you need only press out the comedones or blackheads that appear at the side of the nose. They are declared to be the same creature.

Our story of larvae and worms prepares us to encounter unpleasant folkbeliefs about still stranger lives that are said to be lived in this *corpus vile* of ours. There are to be found among unschooled Italians persons who seem to have no more knowledge of the interior of their bodies than the ancient Romans, with a few exceptions, used to have. They picture the existence in themselves of channels and open spaces through which living creatures of visible size can move about freely without harm to themselves, of which, fortunately for our comfort, the science of anatomy knows nothing. This picture of man's interior justifies a fear that members of the animal kingdom may enter the body through the mouth to stir up all manner of trouble; flies to lay eggs that produce worms in the lungs or stomach, a snake which slips into the stomach of a nursling or its mother's to live comfortably on the milk or other food that they ingest.[59] It is an ungrateful beast: by its squirming and its biting, it keeps its benefactor constantly upset.[60]

Italians who are quite ignorant of the part that fleas, lice, bugs, and ticks play in causing disease and quite indifferent to sanitary measures for the suppression of insect-carriers may yet assure you that an insect can make its way through the ear directly into the brain,

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The belief is by no means, of course, confined to Italy; cf. Morris Fishbein, *Shattering Health Superstitions*, 233. See, also, E. Berdoe, *The Origin and Growth of the Healing Art*, 414–415; Benjamin L. Gordon, *The Romance of Medicine*, 8; William G. Black, *Folkmedicine, A Chapter in the History of Culture*, 32–33; Notes and Queries, Ser. 5, V (1876), 24; 155; 476; VI (1876), 97. The Chinese had this notion centuries before the Christian era. The ancient Egyptians and Assyrians recognized this toothworm as the personification of an evil spirit that had taken possession. It was natural for those who believed in magic to resort to the use of earthworms boiled in oil as a cure and to put worms of other sorts in cavities caused by decay (*N. H.* 25.171; 30.23–24; cf. 27.89). Maggots found in filberts have been used in modern times (Bostock and Riley, *Transl. of Nat. Hist. of Pliny*, V, 431 note 54). See on the topic B. R. Townsend, "The Story of the Tooth-worm", *Bulletin of the History of Medicine*, XV (1944), 37–58, and especially Scrib. Larg. *Compos.*, 10, 54, and, for the later belief in the toothworm, Vincenzo Guerini, *History of Dentistry*, 125; 141; 148; 150; 153; 158; 199; 203; 214; 220; 228–229; 231–232; 247; 268; 307; 309.

[54] Z. Zanetti, *op. cit.*, 180–181.

[55] C. Coronedi-Berti, *Appunti*, 10.

[56] G. Bastanzi, "Superstizioni religiose nelle provincie di Treviso e di Belluno", *Archivio per L'antropologia e la etnologia*, *XVII* (1887), 272; cf. Z. Zanetti, *op. cit.*, 180.

[57] Z. Zanetti, *op. cit.*, 8.

[58] Z. Zanetti, *op. cit.*, 8; 175; 178.

[59] Z. Zanetti, *op. cit.*, 185.

[60] Z. Zanetti, *op. cit.*, 186.

and, establishing itself there, be responsible for indescribable torture,[61] and that some cases of madness are due to the sprouting of a grain of cereal which has penetrated the nose or ear to enter eventually the brain with its foliage or its roots.[62]

While the idea of an organ in the body moving around in it as a living animal is very old,[63] I can find no clear mention of it in the Latin authors of two millennia ago, but the treatment accorded the uterus or its owner in cases of hysteria must interest us in view of certain ideas which we find current in parts of modern Italy about its vagrancy.

It helps us to realize how mysterious some of the functioning of a womb must have appeared to an ignorant Roman when we read for example, in the *Historia Naturalis* of Pliny the Elder, what he mentions as a generally agreed upon fact, that if a pregnant woman stepped over an egg of a raven, she would inevitably miscarry by the mouth.[64] It must, of course, have been a matter of general knowledge in antiquity that a woman's womb was to a certain extent mobile and subject to serious displacement.[65] Cases of prolapsus would provide sufficient ocular evidence of this. Then, too, as being the container and nourisher of the embryo, the organ could readily seem to be endowed with a certain life of its own. How independent this might be of the life of the female herself, how free the womb was to move about contrary to her will and comfort could puzzle any man, not to say any woman of two millennia ago to decide.

If a woman who is undergoing an attack of hysteria is ignorant of all scientific knowledge, she cannot be expected to recognize her sensation of choking, as if she had a lump in her throat, as merely the result of a spasm of the esophagus and pharynx. She might more naturally conclude that her globus hystericus, as the doctors so aptly term it, was a certain lively organ of hers which had come up from below and needed to be sent back again. Obviously the course to follow was to make it as unpleasant as possible for the intruder to remain. As a matter of fact, a Roman physician used various more or less vile-smelling things to cure hysterical suffocation. Prominent, even then, among the remedies was that oily product of the anal glands of the beaver which went by the name of *castoreum* in those times, as it often does now.[66] According to vulgar opinion, castor was a testicular product, and we have a quaint story[67] that the beavers knowing that it was only in order to secure this valuable substance that the huntsmen pursued them, would castrate themselves by a bite, surrendering their testicles as a peace offering, an act of appeasement that proved to be as futile as in some historical mistakes that need no mention here, since the emasculation, as such a sign of weakness should, cost the poor beasts their life.

We may note that the hysterical patient was not only given the castor to smell, as in modern therapy, but might also be fumigated with it from below, or receive it as a suppository.[68] So great was the power of the beaver's fluid over a female that even to hold it over the head of a pregnant woman would threaten her, it was said, with a miscarriage, while if she stepped over the stuff or over a beaver itself, abortion was sure to occur.[69] The existence of this superstition must not tempt my reader to believe that beavers were so commonly recumbent in the thoroughfares

[61] Z. Zanetti, *op. cit.*, 187.

[62] Z. Zanetti, *op. cit.*, 187, note 1.

[63] Many popular works on medicine deal with the belief in a migrant womb: cf., *e.g.*, Palmer Findley, *Priests of Lucina, The Story of Obstetrics*, 33; 41; 63; Edward Berdoe, *The Origin and Growth of the Healing Art*, 185; D. McKenzie, *The Infancy of Medicine, An Enquiry into the Influence of Folk-Lore upon the Evolution of Scientific Medicine*, 286: Plato, Aristotle, and perhaps Hippocrates. *Ebers Papyrus*, 288. See B. L. Gordon, *op. cit.* (see note 53), 56.

[64] *N. H.* 10.32–33; 30.130. On the belief that the polecat brought forth its young by the mouth: T. Dunglison, *History of Medicine from the Earliest Ages to the Commencement of the Nineteenth Century*, 100.

[65] Cf., e. g., *N. H.* 7.175; 11.209.

[66] Lucret. 6.794–796; *N. H.* 32.101; 32.132.

[67] *N. H.* 8. 109; 32.26.

[68] *N. H.* 32.28; 32.132; 32.134.

[69] *N. H.* 32.133.

of Rome as to be a factor in the birthrate of the city.

Besides *castoreum* our classical writers mention other remedies which anticipate our smelling-salts, sternutatories, antispasmodics, and the like which served to stimulate or shock the olfactory nerves, vinegar, garlic, onion, pepper, hellebore, unscoured wool, seal oil, burning pitch, and the extinguished wick of a lamp.[70] The doctor might also give the hysterical woman a pretty dynamic fumigation by setting fire near her to such things as the callosity of the purpura, gastropods extracted from conch shells (*strombi*), which had been allowed to putrefy in vinegar, the fetid gum resin galbanum, lint that had been greased with fat from a dolphin, hair, horn, and sulphur.[71] The rennet of a seal was used as a pessary.[72] Sometimes a mere dousing with cold water would mend matters, they thought, for a wretched patient.[73]

Let us now turn to the Italy of our time and see how much of the animal kingdom some of the more ignorant inhabitants can visualize in themselves when imagination takes its full-fledged flights.

Of intestinal worms and the treatment that was accorded them in both periods of history enough has been said, and we now have sufficient background in our account of the Roman doctoring of hysteria to make more interesting and understandable certain Italian popular beliefs about the womb.

Speaking more particularly of the people in and around Perugia, Zeno Zanetti informs us that this organ is likely to get the blame for any nervous disturbances whatsoever in an ailing woman. According to one superstitious idea, except during the period of a woman's gestation, the womb is itself a polycephalic animal. It has seven heads like a hydra. Its tastes are capricious, so that it has to hunt around in the chest and abdomen to find both the food and the odors that it enjoys.[74] Elderly dames of the community who have made themselves trustees of the folklore on uterine troubles advocate infusions of various herbs as medicaments for calming the ferocious beast, among them feverfew or wild chamomile (Matrecaria parthenium) and ordinary chamomile (Matricaria camomilla). Both of them should be picked on the Day of St. John in order to insure for them their maximum of magic potency. According to the teachings of the masters of occult lore, camomilla must be gathered with the left hand and not allowed to touch the ground before it is brought into the house.[75] The Latin name *matricaria* itself suggests its use in easing the pains of the matrix.[76] When a hysterical woman is suffering from ischuria, i.e., retention or suppression of her urine, merely urinating on one of these plants is expected to relieve her.[77] Other folk prescriptions for hysteria are sweet, garden, or knotted marjoram, Origanum majorana, the pungently aromatic herb that Italians call *maggiorana*, and mint, Mentha viridis.

When the uterine animal is angry, it can cause the throat to contract and the woman to fall to the ground. Convulsions, hysterical outcries, fits of fainting, "nerves" are to be attributed to its unruly movements. It can even kill its host.[78] Since it has different tastes in different individuals, as is shown by those of the person in which it lives, one woman will not be able to endure a certain food or odor which may be aggreable enough to another, because in her case this stirs up the uterus; sometimes the "beast" *fa l'inferno*, i.e., "plays hell" with the interior, and throws the viscera into a topsy-turvy state. During the paroxysm of the fit of suffocation caused by the uterine monster, those who are knowing in such matters run to the victim's assistance

[70] Cels. 4.27.1B; cf. 3.20.1; *N. H.* 32.130.

[71] Cels. 4.27 1D; cf. 3.20.2; *N. H.* 28.70; 32.129; 32.134.

[72] *N. H.* 32.130.

[73] Cels. 4.27.1B.

[74] Z. Zanetti, *La medicina*, 10; 81; Encic. ital. s.v. "*Medicina*".

[75] G. Ferraro, *Botanica*, 168.

[76] C. Coronedi-Berti, *Appunti*, 10. An ancient precept: matrix sequitur odorifera et fugit foetida.

[77] Z. Zanetti, *La medicina*, 83.

[78] Z. Zanetti, *op. cit.*, 81.

with a lighted oil lamp in the flame of which they burn some of her own hair or else a bit of wool. They give her nose the full effect of the stench. Thereupon the ill-behaved animal, scenting the repulsive odor, descends once more into the abdomen, leaving the throat free. This restores the natural breathing of the woman.[79] A prolapsus of the womb should be corrected by a fumigation which is accomplished by burning feathers, greasy rags, and pieces of an animal's hoof. An alternative is to use topically malodorous applications and fomentations.[80] Until some of the repellants have driven the womb into its proper place, a young woman may figure in local gossip as an *ermafrodita*, and to be bisexual is not reckoned a matrimonial asset. Much of this therapy reminds us of what we found the ancient doctor using for hysteria.

Another creature which some ignorant Italians believe occasionally makes its home in a woman is a tiny little animal, *piccolo animaletto*, which lives in the womb. Appropriately enough it is called a *tarpa*, *tarpa*, or *talpa* being the Italian word for that tiny-eyed excavator, the mole.[81] According to an ancient belief, but one that is made no more comforting by its antiquity, the uterine *tarpa* actually looks not so much like a mole as like a bat, a *pipistrello*. It is responsible for pains in the womb, and it devours the fruit of conception as soon as it is barely formed, thus keeping a woman sterile so long as she plays host to it.[82] Those who believe in the existence of these creatures identify them somehow or other as the solid clots which in a natural miscarriage come from the womb with the mola or mole, this medical term meaning, of course a "mass", not a "mole" of the animal world. The local wise woman will prescribe metallic mercury internally as the means to kill a *tarpa*.[83] But there is always the possibility that, if her advice be taken, guest and host may both pass out together.

We learn that there is another terrible animal which can be loose in the body of a member of either sex, the *cancro* or "cancer".[84] It manifests all the characteristics of a carnivorous beast: it bites, tears, and devours. Therefore, whoever would make it spare the flesh of the person in whom it dwells will see to it that it is fed on meat every day. The name *cancro*, which is the Italian word for crab, suggests explanations for some of the fancies that are current about its nature and behavior. Persons who pretend to knowledge of it distinguish between a male and a female beast. It is a male if the cancer returns after it has been removed. The raw meat fed to it, if it is an internal cancer, goes to it of course, through the mouth of the patient; if the growth is external, one should apply to it pieces of lean flesh from a calf or some other meat.[85]

So ends our story. If we are inclined at times to smile at the old Romans, or at their more direct descendants who have perpetuated some of their nonsense, we should remember that similar pictures could be painted for any other people in the world. Perhaps a time may never come when the imagination of somebody cannot conjure up a monstrous parasite or a cruel tenant housed as comfortably within the human body as Jonah lived in the belly of the whale. The practical problem is still to discover the best ejective medicine. While the best science of our time could not have done much for the poor whale, even the Romans of two millennia and more ago knew how to expel worms.

[79] Z. Zanetti, *op. cit.*, 83.
[80] Z. Zanetti, *op. cit.*, 244–245.
[81] Encic. ital., s. v., "*Medicina*".
[82] Z. Zanetti, *op. cit.*, 9.
[83] Z. Zanetti, *op. cit.*, 97; 118.
[84] Z. Zanetti, *op. cit.*, 9; G. Pitrè, *Medicina*, 265–266.
[85] Z. Zanetti, *op. cit.*, 209–210.

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Meeting, October 10, 1946

Marble Bone Disease; a Study of Its Relation to Normal Bone Development. Carla Zawisch. (*Abstract 1, below.*)

Further Studies on the Pathogenesis of Polycystic Disease: Reconstructions of Cystic Elements from the Liver, Pancreas, and Lung. Robert F. Norris and Ralph M. Tyson. (*Abstract 2, below.*)

Histological Lesions in Purpura Hemorrhagica. T. K. Rathmell. (*Abstract 3, below.*)

Meeting, November 19, 1946

Early Reactions of the Lungs of Rabbits to Inhaled Virulent Bovine Tubercle Bacilli. H. L. Ratcliffe and W. F. Wells. (*Abstract 4, below.*)

Some Chemical Factors Concerned in the Maintenance of Cell Adhesiveness. Irving Zeidman. (*Abstract 5, below.*)

The Pathology of Infectious Mononucleosis. R. P. Custer and Edward B. Smith. (*Abstract 8, next issue.*)

Meeting, December 12, 1946

Degenerative Changes in Tumor Cells Induced by Bacterial Polysaccharides. Irene Corey Diller. (*Abstract 6, below.*)

The Use of Plants in the Study of Cancer. Philip R. White. (*Abstract 7, below.*)

Meeting, January 9, 1947

The Treatment of Lymphoblastic Leukemia with Crude Myelokentric Acid. F. R. Miller, H. W. Jones, and P. A. Herbut. (*Abstract 8, below.*)

The Influence of Sex Hormones upon Hepatic Lesions Produced by 2-Acetaminofluorene. Joseph Stasney, A. Cantarow, and Karl Paschkis. (*Abstract 9, below.*)

Abstracts

Abstract 1

Marble Bone Disease; a Study of Its Relation to Normal Bone Development. Carla Zawisch.

Marble bone disease (osteosclerosis fragilis generalisata, Albers-Schönberg) is caused by an agent as yet unknown which acts on the bone-forming mesenchyma during the second period of its differentiation. The partly differentiated bone tissues characteristic of this period become hyperplastic, and further differentiation is greatly retarded. The malformation is responsible for the general retardation of resorption, because the two phases of the bone-forming process—deposition and resorption—condition and stimulate each other. In marble bone disease, the threshold of response to stimuli which bring about resorption, is raised. Resorption of the corticalis on the surface of the marrow cavity is arrested completely for a long time and the marrow cavity preserves its fetal size and shape. The corticalis becomes abnormally thick because none of the earlier strata are completely removed. The same processes are responsible for the abnormal amount of spongiosa present in marble bones. If the individual survives long enough, normal differentiation takes place and interior resorption tends to make up for the former deficiency.

The hyperplasia and persistence of less differentiated bone types in the metaphyses is responsible for the expansion of the ends of long bones known as clubbing. All the various

bone tissues, including lamellar, are also pathologic in their finer structure. They are e.g. poorer in fibrils than normal and this has a bearing on the calcium content of marble bones.

Abstract 2

FURTHER STUDIES ON THE PATHOGENESIS OF POLYCYSTIC DISEASE: RECONSTRUCTIONS OF CYSTIC ELEMENTS FROM THE LIVER, PANCREAS, AND LUNG. Robert F. Norris and Ralph M. Tyson.

The gross and microscopic lesions of polycystic disease in the livers of 2 cases, in the pancreas of one case, and in the lungs of 2 cases are described. By means of serial sections, some of the cystic lesions of each case were reconstructed and are demonstrated.

The lesions in general correspond to those previously described by Norris and Herman in polycystic disease of the kidney and it is believed that the sequence of anatomic changes are similar in polycystic disease of all organs.

It is concluded that in polycystic disease the lesions begin in the fetus. The essential lesion is segmentation of the epithelial ducts of a glandular organ which occurs after differentiation of the involved structures and which does not prevent the relatively normal differentiation of the glandular or functional part of the organ usually situated distal to the segmenting ducts. Persistence of isolated segments of ducts as cysts explains the occurrence of polycystic disease following birth. The process of segmentation is a degenerative one and is analagous to the normal resorption of provisional structures during embryonic life. In polycystic disease, therefore, the involved organ is more or less abnormally provisional because the segmentation of the epithelial stalks serves to disconnect some or all of the functional units of the organ from the rest of the body. The cause of polycystic disease must lie in the germ plasm.

Abstract 3

HISTOLOGICAL LESIONS IN PURPURA HEMORRHAGICA. T. K. Rathmell.

The case was encountered among service personnel from the recent conflict. A white male of about 26 years was admitted with a diagnosis of gastric neurosis. Subsequent studies showed delayed syneresis, prolonged bleeding time and thrombocytopenia. Treatment was ineffectual.

Autopsy lesions encountered were gross cardiac purpura, "ball" hemorrhages of the cerebrum, capillary thrombi and endothelial hyperplasia of vessels in the pons, kidney and mesenteric lymph nodes with erythrocytic and megakarocytic hyperplasia of the bone marrow.

While no new entities were encountered the capillary thrombi were unusual. Baehr, Klemperer and Schifrin described them in 1936. They were again noted by Altschule in 1942 and by Bernheim in 1943. Klemperer regards the capillary lesions as platelet thrombi.

The case was reviewed to again demonstrate the histological lesions which may be encountered in certain cases of the clinical syndrome we now designate as "Purpura Hemorrhagica".

Abstract 4

EARLY REACTIONS OF THE LUNGS OF RABBITS TO INHALED VIRULENT BOVINE TUBERCLE BACILLI. H. L. Ratcliffe and W. F. Wells.

Apparatus and techniques developed in the course of studies on airborne infection and disinfection, permit infectants to be implanted upon alveolar tissues of the lungs quantitatively and the development of disease processes to be observed from the time of such implantation. Under the conditions of these experiments organisms are transported to and deposited upon lung tissues by natural respiration.

Histologic study of the lungs of rabbits which had inhaled some 20 thousand virulent bovine tubercle bacilli of the Ravenel strain, airborne as single cells, has revealed that the organisms are first taken up by "alveolar macrophages". During the first week of infection the organisms grow within these phagocytic cells without exciting visible change in the tissue. Usually the infected macro-

phages are found as single cells in otherwise normal alveoli.

During the second week of infection growth of the organism is accompanied by increased numbers of the macrophages, which form clusters within alveoli. Late in the second week of infection polymorphonuclear leukocytes and small monocytes become increasingly numerous about the infected macrophages. With further enlargement of the lesions degenerative changes appear within the infected cells. By the beginning of the third week, the focal points of reaction usually occupy several contiguous alveoli and take on the appearance of typical tubercles. Animals inhaling this number of organisms invariably died during the fourth week of infection, the lungs containing myriads of small tubercles distributed uniformly throughout the tissue.

From these studies it is concluded that the primary response of the rabbit's lung to tubercle bacilli inhaled as single cells is the same as the reaction to any other foreign material inhaled in particulate form. Disease occurs only when the organisms in any one focus reach numbers sufficient to excite inflammation.

Abstract 5

Some Chemical Factors Concerned in the Maintenance of Cell Adhesiveness. Irving Zeidman.

Experiments were designed to determine the chemical factors concerned in the adhesiveness of buccal epithelial cells. Cells were separated by micromanipulation and the force required to do this was measured. Normal values for adhesiveness were first determined by separating cells in balanced salt solution. Adhesiveness diminished in calcium-free, magnesium-free, and combined calcium-and-magnesium-free salt solutions. The decreased adhesiveness occurring in a calcium-free solution was irreversible in the sense that restoration of calcium did not restore adhesiveness. Multivalent cobalt ions were ineffective in replacing calcium. An excess of potassium ion did not alter adhesiveness. The spreading factors—hyaluronidase, ascorbic acid, and oxidized ascorbic acid—did not affect the adhesiveness of epithelial cells. It is concluded that calcium and magnesium are essential for the stability of the intercellular cement substance. Since cells of squamous cell carcinoma have low adhesiveness, and since these cells have been demonstrated deficient in calcium, it is suggested that the decreased adhesiveness of the cancer cells is due to a calcium deficiency.

Abstract 6

Degenerative Changes in Tumor Cells Induced by Bacterial Polysaccharides. Irene Corey Diller.

A bacterial polysaccharide isolated by Shear and co-workers from Serratia marcescens is found by them to produce gross hemorrhage and necrosis in mouse tumors when injected intraperitoneally into the host. Cytological studies of the effects of this substance on transplantable mouse sarcomas reveal marked cellular (particularly nuclear) changes in tumor tissue following the intraperitoneal injection of 0.01 mg. per mouse. A progressive series of structural alterations culminating in destruction of the nucleus reaches a maximum around 6 hours post-injection. Resting cells appear relatively unharmed but are inhibited from undergoing division for about 3 days. In a significant number of cases no viable tumor cells could be detected by our methods three days after treatment with a dose that killed 20 to 30 per cent of the mice. When polysaccharide was combined with X-rays this number was increased three-fold. Repeated treatments did not produce greater amounts of destruction, indicating that the tumor, or its host, had become resistant to the bacterial agent. In primary neoplasms, including human sarcomas, the effects were similar to those produced in mouse tumors, but the substance is highly toxic to humans and the dose which could be administered was proportionately much smaller and the amount of tissue which could be made to react was correspondingly reduced.

Abstract 7

THE USE OF PLANTS IN THE STUDY OF CANCER. Philip R. White.

Since cancer is essentially an aberrance in cellular morphogenesis this particular type of aberrance has the same basic significance in whatever organism it may occur. Plants, under some circumstances, may show this sort of aberrance. Three types of plant tumors were discussed: 1) the hereditary tumors of tobacco, 2) crown-gall tumors of sunflower and periwinkle, both primary and secondary, and 3) tumors induced by the action of an attenuated strain of bacteria combined with a growth hormone. All three types are bacteria-free and transplantable in series from host to host and the first is regularly fatal in its primary host. The similarities of these growths to cancer in animals and man were discussed briefly. It is believed that an intensive study of these materials may give valuable information on the nature of cancer.

Abstract 8

THE TREATMENT OF LYMPHOBLASTIC LEUKEMIA WITH CRUDE MYELOKENTRIC ACID. F. R. Miller, H. W. Jones, and P. A. Herbut.

Crude myelokentric acid was extracted from the urine or feces of patients with chronic myeloid leukemia.

The material was emulsified with alkaline water at a pH of 7.5. After sterilization it was given to eight patients with lymphoblastic leukemia. This was done in an effort to stimulate myeloid proliferation, and to try to bring about remissions.

Thirteen partial remissions occurred in treating the eight patients. These consisted of diminution of the size of lymph nodes and spleens, improved appetites and increase in body weight, as well as peripheral blood changes. A shift from a lymphoblastic to a lymphocytic blood picture occurred and was followed by a moderate to marked leukopenia, and then the appearance of myeloid cells, including reticulocytes and platelets in the peripheral blood.

Eventually seven died and five necropsies were obtained. All organs exhibited less leukemic infiltration than untreated cases. The infiltrations were not uniform as in lymphoblastic leukemia but exhibited considerable pleomorphism, an increase in reticulum cells, reticulum and also a few cells resembling Sternberg cells. The bone marrows appeared almost hypoplastic but showed some normal hematopoiesis and all organs exhibited a "washing out" of lymphoid elements.

Summary: Partial remission occurred in all cases with this therapy. The necropsy material was compared with that from four untreated cases. The findings in the treated cases add weight to the belief that the crude myelokentric acid was a factor in bringing about the remission.

Abstract 9

THE INFLUENCE OF SEX HORMONES UPON HEPATIC LESIONS PRODUCED BY 2-ACETAMINOFLUORENE. Joseph Stasney, A. Cantarow, and Karl Paschkis.

2-Acetaminofluorene is known to be a carcinogen which induces a great variety of malignant growths. Malignancy of the liver, breast, bladder and external auditory canal were observed in rats fed 2-acetaminofluorene for 174–375 days. Exogenous and endogenous sex hormones given simultaneously with the carcinogen intensified and accelerated the cystic and neoplastic hepatic lesions induced by 2-acetaminofluorene.

In the target organs rendered hyperplastic by the respective hormones, no tumors occurred in contra-distinction to the high incidence of tumors of the thyroid in rats receiving thiouracil simultaneously with the carcinogen.

The fact was pointed out that the hyperplasia induced by the sex hormones is a functioning hyperplasia, whereas that induced in the thyroid by thiouracil is functionless, may possibly be a determining factor in the relationship between simple and neoplastic growth of tissue.

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Surgical Treatment for Cardio-Vascular Malformations*

By ROBERT E. GROSS, M.D.

IT is an honor to come before the College of Physicians of Philadelphia to present the Fifty-seventh Mary Scott Newbold lecture. The topic to be discussed tonight represents a new field of surgical endeavor and could not have been presented a decade ago, since the first successful correction of a congenital cardiovascular defect was made in 1938. Surgical treatment for malformations of the heart and great vessels comes as a natural sequence in the advance of modern American therapy. Vascular surgery in this country has had a solid foundation in the many studies and contributions of Matas, Halsted, Carrel, and others. Thoracic surgery has made extraordinary progress in the last twenty years, and now it is not surprising that vascular abnormalities within the chest rightfully claim the attention of qualified surgeons. In a brief way I would like to present the salient features of four different types of intra-thoracic cardiovascular malformations, indicating in each instance some of the hazards of the untreated condition, the points whereby the lesion can be recognized, the methods for surgical attack upon the problem, and the results obtained by such surgery.

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PATENT DUCTUS ARTERIOSUS

The possessor of a patent ductus arteriosus may tolerate this abnormality through a long and active life if the shunt happens to be a small one and if the individual is fortunate enough to escape a superimposed infection. In general, the main hazards of an open ductus are three-fold. 1. If the ductus is of large size, much blood can be diverted from the peripheral circulation so that the child's physical development is retarded. 2. If the ductus is of considerable size, an extra burden is placed on the heart which can become a significant factor leading to cardiac fatigue or even failure in mid-adult life. 3. Superimposed *streptococcus viridans* infection is found in approximately twenty-five per cent of those individuals who live well into adult life. This last complication used to carry a high fatality rate, but with modern penicillin therapy the seriousness of such infection has been greatly diminished.

The best studies on the prognosis for individuals with an untreated patent ductus arteriosus have been made by Keys and Shapiro (14). They have found that humans who are alive at seventeen years of age with an open ductus have a life expectancy beyond this which is only about half that of the population as a whole. It becomes apparent that the patent ductus arteriosus often seems to be a benign abnormality when observed in childhood, but that ultimate incapacitation and shortening of life are apt to be brought about by the malformation. It is this general picture which has given impetus to the development of surgical methods for closing the ductus; we hope to prevent complications before they have appeared and, in other patients, we must treat complications which have already occurred.

A patent ductus arteriosus can usually be recognized with ease. The picture may be somewhat distorted in the first two or three years of life, and also in adult life when there is associated cardiac failure, but aside from these two circumstances a few simple observations can establish the diagnosis with accuracy. There is no cyanosis, clubbing, or polycythemia. Some patients have a retarded physical development, particularly when the ductus is of large calibre. In young children there is rarely evidence of cardiac fatigue, whereas in older children and adults some dyspnea, moderate limitation of activities, or more frank evidence of cardiac failure are apt to be found, particularly if the ductus is large and the burden on the heart is great. The activity of the heart is not greatly increased in the presence of small shunts, but it is markedly augmented when they are large. The murmur has a characteristic sound, and should rarely be confused with those originating from other defects. It is most intense in the second or third interspace to the left of the sternum. It is continuous throughout the cardiac cycle, has a systolic accentuation, and dies off in diastole. In a few instances it is slightly more intense in diastole than it is in systole. It is very rare for the murmur to be limited to systole. It has a peculiar, rumbling quality which has been responsible for its characterization as a "machinery murmur". When the shunt is large and the murmur is loud there is apt to be an associated thrill; this may be continuous in time or may be limited to systole. The diastolic blood pressure is within a normal range if the leak is small, but it is lower than normal in the presence of large ductal shunts. Electrocardiographic tracings are helpful, particularly from the negative evidence which they generally give. In most cases there is no important variation from the normal. Occasionally there is a left-axis shift, whereas a right preponderance is extremely rare and should arouse one's suspicion regarding the probability of some other type of cardiac defect. In only two instances have I seen a right-axis deviation from an uncomplicated ductus arteriosus (both of these electrical axes returned to normal after surgical closure of the ductuses). Roentgenologic studies should always be made, utilizing both film and fluoroscopic observations. When the ductus is small, the roentgenological picture will show little or no important variation from the normal. Conversely, a large shunt between the aorta and pulmonary artery will bring about definite changes among which are the following: The heart is slightly or moderately enlarged, marked increase in size being rare. The hypertrophy (or dilatation) is most apparent in the left ventricle and left auricle. The heart is over-active and has an abnormal forcefulness of beat. The pulmonary artery is more full than normal and has a greater amplitude of pulsation. In about half of the cases the arteries of the lung roots have a "hilar dance". The vascular markings throughout the lung fields are usually increased.

Techniques for closure of a patent ductus arteriosus have been extensively described elsewhere (5, 6, 7), and only a few comments will be given here regarding operative details. The original approach which I described for exposure of a ductus has withstood the test of

time, and I see no reason for changing it in favor of a lateral or posterior wound. The opening is made with a left antero-lateral, submammary wound, entering the thorax through the third interspace, and dividing the second and third costal cartilages so that the ribs may be separated. The left pleural cavity is traversed so that the mediastinum can be viewed from its left, antero-lateral aspect. If properly made, this wound gives sufficient room for safe performance of the subsequent steps. The ductus is now brought into view by sharp and blunt dissection of surrounding structures. In young patients this is not a difficult matter, but in older subjects the increased vascularity of the region, the loss of resiliency in the neighboring aorta and pulmonary artery, and the fibrous adherence of structures (in the region of a fistula) may make the undertaking tedious and time-consuming.

Methods of obliteration of a ductus have undergone several evolutionary stages. In a total of two hundred personally treated cases, forty-three individuals had some form of ligation. Follow-up observations indicated that in about eighty per cent a complete and permanent closure of the ductus was obtained. In about ten per cent, the ligature cut through in a few weeks following operation and some of the fistula was re-established. In the remaining ten per cent, the ligatures were not put on tightly enough to close the vessel completely. While these over-all results were fairly good, an attempt was subsequently made to improve the surgical treatment by devising a method whereby the ductus could be completely divided. In the last one hundred and fifty-seven patients, varying from one to forty-seven years of age, the ductus has been severed so that the pulmonary artery and aorta could be separately closed.

In this latter group there have been four fatalities (one from sepsis, one from poor anesthesia, two from cardiac failure). This gives a mortality rate of 2.6 per cent. There has been no fatality from hemorrhage (at operation or subsequent thereto) in the division cases. (In the period during which the one hundred and fifty-seven patients had ductal division, I have explored two other individuals who had such a large ductus or advanced, regional-vessel sclerosis that division or ligation could not be done.) The results of complete division of the ductus have been so satisfactory that I have now completely abandoned all forms of ligation of the vessel. The complete division technique insures that all of the leak is closed off and that there is no chance for its re-establishment. These operative procedures are tolerated extremely well and post-operative hospitalization is rarely longer than ten or twelve days.

An adequate number of patients have now been operated upon and sufficient time has elapsed since the performance of these procedures to give a clear and satisfactory evaluation of surgical closure of the patent ductus arteriosus. Our series has included many children with good cardiac reserve, but it likewise included a considerable group of older subjects with complications such as cardiac fatigue or superimposed infection which greatly increased the operative risk. In one patient there was a concomitant, rheumatic mitral-stenosis and insufficiency and in four others there were septal defects. In these five patients the cardiovascular apparatus obviously could not be returned to a normal state, but closure of the ductus was believed to be worthwhile in reducing the cardiac burden.

A review of records and a re-study of patients from one to nine years after operation gives a very bright view of what can be accomplished by surgical closure of the patent ductus arteriosus. The diastolic pressure, if previously low, is immediately restored to a normal level. In the vast majority of cases all murmur has disappeared. In the five cases with associated lesions, the loud ductus murmur has disappeared and the murmur produced by the associated lesion has remained. In the earlier cases when ligation alone was performed there were occasional disappointments which resulted from an incomplete closure of the

fistula, or from a partial recurrence of the same. Since adoption of the complete division technique it is very rare to have any post-operative murmur, but in a few instances there has been a faint, evanescent, systolic, pulmonary murmur which was believed to be functional in nature. Following closure of a ductus of Botalli, the same cardiac changes are apparent which have long been observed following obliteration of any large arteriovenous fistula: a heart, which before operation had a very heaving and pounding impulse, will be found to have a post-operative activity which in comparison is quiet and much less vigorous. In those individuals who have had physical retardation before operation we have seen a gratifying gain in weight during the post-operative period. Many children have added twenty-five to thirty per cent to their weight during the year or year and a half following operation. Direct measurements have been made by Eppinger, Burwell, and Gross (4) on patients before and after closure of the shunt and data obtained which clearly indicate that the work of the heart is tremendously reduced by shutting off the arterial leak; obviously, the cardiac reserve is increased to an important degree. Finally, it was demonstrated by Touroff and Vesell (17) that in the presence of *streptococcus viridans* infection, surgical closure of the ductus (under certain circumstances) has very beneficial effects on the course of the infection. In our series there were ten patients with such superimposed infection, and following closure of the ductus seven of these have been permanently cured (all in the pre-penicillin era). You are fully aware that the same general results can now be obtained with penicillin alone. While we must recognize the potency of penicillin in eradication of these infections, it is well to point out that some patients (even though cured of infection) have serious cardiac damage or subsequently die of cardiac failure. Hence, it is quite probable that the optimum therapy of the future will combine the anti-biotic use of penicillin with the reduction of cardiac work which can be obtained by surgical closure of the ductus.

TETRALOGY OF FALLOT

For many decades cardiologists and pathologists have been recognizing the tetralogy of Fallot, and have placed considerable emphasis upon the anatomical defects which are known to exist in this malady. More recently, Dr. Helen Taussig (1) has emphasized the *physiological* aberrations and has pointed out that two fundamental disturbances account for the cyanosis and debilitating effects of this state. First, there is some inter-mixture of oxygenated and unoxygenated blood because of the dextro-position of the aorta—which receives blood from both the left and right ventricles. Nothing can be done by surgical means to correct this inter-mixture. Second, there is a diminished flow of blood into the lungs because of the narrowing (or complete blockage) of the pulmonic valve or of the infundibulum just below it. With this reduced flow through the lungs, the blood is not able to take up sufficient amount of oxygen to fulfill the needs of the body. This latter physiological defect can be overcome to some extent by the surgical establishment of a shunt between the aorta and pulmonary artery—to allow more blood to pass into the lungs. It is this fundamental concept which lies behind all of the operative procedures which have been proposed and carried out by Blalock (1, 2).

It must be pointed out that not all individuals with cyanosis from birth have a tetralogy of Fallot. There are many other serious cardiac derangements, and many of these lead to fatality within the first few weeks or months of life. A child who survives beyond the second year, and who has persistent or transient cyanosis may still have a defect such as a common truncus, cor-triloculare, an Eisenmenger complex, a deficiency in the oxygen-carrying mechanism of the blood, etc., but yet there is about a seventy-five per cent chance that the patient has a tetralogy of Fallot.

Subjects with a tetralogy show cyanosis of

variable intensity, clubbing of variable extent, polycythemia which may be marked, and always some invalidism which is apt to be of moderate or marked degree. These patients have a great diminution incapacity to tolerate exercise and in severe cases they spend the greater part of their waking hours in assuming a squatting position, which for some poorly understood reason brings them maximum comfort. The polycythemia and high hematocrit constantly impose the hazards of thromboses in various parts of the body, particularly in the central nervous system where they may lead to bizarre and extensive neurological damage, hemiplegia, speech defect, or even death. The anatomical and physiological derangements within the heart and great vessels appear within wide range, and hence it is not surprising that the clinical picture varies greatly from case to case.

Uniformly, these patients show a right-axis deviation in the electrocardiographic tracings. To be favorable for surgery, a case must show roentgenographic evidence of a pulmonary artery which is distinctly smaller than normal and lung fields which are not congested. Cardiac catheterization gives important information regarding the disturbed physiology, but it is particularly helpful in providing direct measurement of the pulmonary artery pressure. A pulmonary pressure which is lower than normal probably indicates that there is a small pulmonary flow and hence suggests that the establishment of an aorta-pulmonary artery fistula will be beneficial.

Blalock has devised several methods for producing a channel between the aorta and the pulmonary artery to increase the pulmonary blood flow. Either subclavian artery, a common carotid artery, or an innominate artery may be severed and its proximal end turned downward for anastomosis to the pulmonary system. While the larger shunts appear to be more beneficial than the smaller ones, the interruption of the common carotid or innominate artery has carried forbidding risks in the form of cerebral ischemia and post-operative hemiplegia; these have now been largely abandoned in favor of the subclavian artery shunts which carry a much lower risk. More recently Potts, Smith, and Gibson (16) have proposed a method of making a direct opening between the aortic arch and the pulmonary artery. With more extensive experience this method may prove to have considerable merit because it should allow the operator to make a shunt of appropriate size, and furthermore, it would obviate the difficulties of making a union under considerable tension, which is often the case when the subclavian artery is brought down to the pulmonary system for anastomosis.

The results following operations of this type vary considerably. Post-operative intracranial thrombosis can occur even though the common carotid pathways have not been interfered with. Some individuals have a smaller post-operative shunt than appears to be desirable, a fact which is sometimes related to partial thrombosis at the anastomotic site. An occasional individual will succumb from hemorrhage at the suture line of anastomosis or from some other part of the thorax. Some individuals, even though a shunt of considerable size has been established, get only mimimum benefits from the operation—presumably because of the severity of the other derangements such as over-riding of the aorta. While fatalities, occasional failures, and various types of complications are frequent enough to make this seem to be a discouraging undertaking, there can be no question about the fact that the majority of these patients are greatly improved by the operation and frequently show dramatic and brilliant changes following the establishment of such an artificial shunt. There is no chance of restoring a normal cardiovascular arrangement to these people, but this does not detract from the tremendous advance which has been made in bringing to these miserable patients a more normal appearance, a greater capacity for physical exercise, and also a diminution in the threat of thromboses which previously existed because of the polycythemia.

My familiarity with these operative pro-

cedures has been quite limited and I would like to draw upon the experience of Blalock to point out the current results of surgical undertakings in this field. In a rapidly-growing series of patients, 315 have now been operated upon by Blalock (3). The fatality rates have not been excessive, when one considers the desperate condition of many of these people. In the more recent part of his work the death rate has been around fifteen per cent, and for those who had a subclavian anastomosis—which is the generally employed procedure at the present time—the mortality figure has been brought down to about seven and a half per cent.

COMPRESSION OF THE TRACHEA OR ESOPHAGUS BY ANOMALOUS AORTIC ARCH OR GREAT VESSEL

Recently my attention has been drawn to a small group of infants who have had dysphagia or marked respiratory distress because the esophagus or trachea (or both) has been impinged upon by some great vessel in the upper thorax which has had an anomalous structure or has followed an unusual course. Since it is now possible to explore the mediastinum of babies with a fair degree of safety, it is important to recognize these malformations because, under certain circumstances, it is possible to bring relief to such infants.

Dysphagia may manifest itself as hesitation in swallowing, appearance of discomfort during the act of swallowing, spitting up of uncurdled milk shortly after it has been ingested, or refusal to take feedings in any but small amounts. Whenever the possibility of partial esophageal obstruction arises, roentgenographic examination of the esophagus during a swallow of barium can rapidly prove or disprove the presence of such a condition. Fluoroscopic or film studies in the antero-posterior and lateral views will adequately visualize any deformity of the esophageal tube. An anomalous right subclavian artery which has an origin from the left side of the aortic arch will produce a long and oblique indentation on the esophagus running from the left side upward and toward the right. In some instances this is on the anterior surface of the esophagus, but it is much more common for the vessel to run behind the esophagus. In the presence of a double aortic arch, one limb of the arch may run behind the esophagus and produce a transverse defect of the posterior wall of the esophagus. Either of these esophageal defects occur in the general level of the third or fourth thoracic vertebrae. They have been commented upon extensively elsewhere by Neuhauser (15).

In severe forms of tracheal compression, the respiratory rate is increased, the baby obviously has marked distress, there is a loud, crowing noise during inspiration, there is suprasternal and intercostal retraction, and frequently the baby has a tendency to keep the head in marked hyper-extension—a position which stretches out the trachea and tends to push away any extrinsic object which is pressing upon it. Direct laryngoscopy should be performed to make sure that the pathology is not within the larynx itself. The interior of the trachea can be viewed directly through a small bronchoscope, but it is much less disturbing to the baby to omit this procedure and to study the trachea roentgenographically by the instillation of a few cubic centimeters of lipiodol through the larynx and then taking appropriate films in the antero-posterior and lateral projections. Such study can clearly indicate any narrowing, deformity, or displacement of the trachea.

Since expressing an interest in this field, we have come to recognize three types of abnormality, which, when severe enough, can be alleviated by surgical means. Those individuals with a right subclavian artery which presses upon the trachea, or more commonly upon the esophagus, can obtain complete relief from their symptoms by mediastinal exploration and division of this vessel (8). This operation does not diminish the flow of blood to the right arm to any serious degree since there are adequate collaterals in the second and third portions of the subclavian artery. This operation has been undertaken

in three instances and there has been complete relief of dysphagia in each. The second type of abnormality is concerned with an innominate artery which has an unusual origin on the aortic arch, which makes it necessary for the vessel to wind around the anterior and right antero-lateral surface of the trachea to reach its normal exit from the thoracic cage. This makes external pressure upon the trachea and gives considerable respiratory distress. The symptoms can be completely relieved by mediastinal exploration and surgical displacement of the vessel into a more anterior position so that all pressure is taken off of the trachea. The third type of abnormality is found in infants who have a double aortic arch, the posterior limb of which runs behind the esophagus and the anterior limb runs in front of the trachea (9, 18). Five such babies have been seen with some difficulty in swallowing and with marked symptoms of respiratory obstruction. In each instance the anterior limb of the double aortic arch has been smaller than the posterior one and could be divided without producing any important changes in the circulation. One of these children died from a post-operative hemorrhage, and another died twenty-four hours following operation from cerebral degeneration and edema from long-standing anoxemia. The other three patients have had a very satisfactory relief of their respiratory distress. I have no doubt that there will be future descriptions of additional types of vascular malformations which produce tracheal and esophageal compression and which will be treatable by surgical means.

COARCTATION OF THE AORTA

In the so-called "adult" form of coarctation of the aorta there is a narrowing (or complete block) in the upper portion of the thoracic aorta at or near the junction of the ligamentum arteriosum. In childhood this abnormality often escapes detection. In young adult life its presence should always be suspected when seeking a cause for an existing hypertension. Recent studies have been made in the effort to determine the prognosis for patients who have survived the first two years of life and are known to have a coarctation of the aorta. Such patients may be separated into four general groups of about equal size. In the first quarter are those who have had little or no disability during life and have lived to the age of sixty or seventy years or more. In the second quarter are those who have died very suddenly because of rupture of the aorta. Such a catastrophe, if it is to occur, usually takes place in the third or fourth decade of life. In the third quarter are those who have died because of *streptococcus viridans* infection. This threat is, of course, not as serious today when modern chemotherapy, including penicillin is available. In the final quarter are those patients who have died because of the hypertensive state, exitus coming from cardiac failure or from intracranial hemorrhage. About forty per cent of all patients have died between the ages of fifteen and thirty years—a period wherein normal human beings are expected to be in their best physical condition. While some individuals tolerate a mild coarctation over a long period of time, it is undeniable that the possessor of the malformation is faced with profound hazards to his health and life. It is this grave outlook which has spurred my efforts to find a surgical method for treatment of this congenital abnormality.

Coarctation of the aorta is not difficult to recognize. Most important in its detection is the finding of a disparity between the blood pressures of the arms and legs. Normally, the leg pressure should be equal to or above that in the arms, whereas in the presence of an aortic block the pressure in the legs is distinctly lower than that found in the arms. The femoral, arterial pulsations are diminished or absent. The pressure in the arms is frequently elevated, and hypertension of moderate to severe degree is common. Evidence of collateral circulation is usually not found in young children, but in older children and in adults pulsating and tortuous arteries may be found in the supra-clavicular fossae, the infra-clavicular regions, in the infra-axillary areas,

and particularly over the back, below and medial to the angles of the scapulae. Murmurs are variable but in most cases there is a systolic murmur, of only moderate intensity, which is best heard in the left upper portion of the precordium and which is transmitted fairly well to the back. After excitement or mild exercise, the head, neck, and shoulders are apt to flush, whereas the trunk and lower extremities are apt to blanch. Electrocardiographic tracings may show some left-axis deviation, particularly if there is an important hypertension. Roentgenographic examination shows slight or moderate enlargement of the heart, a diminution in size (or absence) of the aortic knob, and notching of the inferior borders of the postero-lateral parts of the ribs. This scolloping is produced by pulsating and tortuous intercostal arteries which are acting as collateral channels. The notching is usually not present in the upper three or the lower three ribs, and usually does not appear until the end of the first decade of life.

Surgical correction of coarctation of the aorta in man rests upon a firm foundation of work from the experimental laboratory. I have previously described the results of investigations (10) which were aimed at finding methods for safe removal of a portion of the thoracic aorta. Working on dogs it was possible to excise segments one and a half to two centimeters in length and to have sufficient stretch in the remaining ends to bring them together for a direct anastomosis and reconstruction of the vessel. Several different types of suture methods were tested and all were discarded in favor of one which consists of a continuous mattress stitch of silk, which grasps the entire thickness of the aortic wall, and turns the ends outward. This brings intima to intima and gives a satisfactory repair, which is seldom complicated by local thrombosis or hemorrhage.

After sufficient practice with these techniques had been obtained from animal work, I felt sufficiently prepared to attempt similar undertakings in human beings for removal of a narrowed segment of the thoracic aorta (11, 12, 13). The approach and exposure are made through the back, with a long incision medial to and below the left scapula, entering the thorax through the bed of the fifth rib. The left lung is temporarily collapsed during the procedure. The narrowing of the aorta has been found near the origin of the left subclavian artery in three instances; in the remaining cases it was below this level. With meticulous care the distal part of the arch and the first portion of the thoracic aorta are freed from their bed. There is no hesitation about placing a clamp on the aorta above and another below the constricted part, since very little blood flows through this area. In most cases, the narrowed part had an internal lumen no more than two or three millimeters in diameter, indeed, in three instances the lumen was completely blocked. After the abnormal segment of aorta is excised and discarded, the remaining ends of the aorta are brought together for an end-to-end suture, following which the clamps are removed. The left lung is completely re-expanded and the chest wound appropriately closed.

To date, eighteen patients have been explored for coarctation of the aorta. In three of them the regional conditions were such that it appeared to be impossible to remove the aortic segment and I decided to withdraw from the chest. In the remaining fifteen patients the coarctation was removed and the aorta was reconstructed; there were two deaths. In one case there was failure to relieve hypertension, because a satisfactory anastomosis could not be established. In the remaining twelve patients there has been a very satisfactory post-operative course, with the appearance of good pulsations in the leg arteries and with a reduction of pressures in the arms to essentially normal levels. An indication of what can be accomplished is shown by Figure 1. The reduction of marked hypertension in this boy has been

ample reward for the exhausting efforts which were required of the surgical team during the operation for removal of his aortic obstruction.

Experience to date would seem to indicate that these operations have a fairly good chance of success and will have a reasonably low mortality rate, when performed in children in the age range from six to eighteen years. During this time the aorta is still elastic and can be worked upon with relative safety. However, beyond the age of twenty years most subjects with coarctation of the aorta develop a relatively high degree of sclerosis in the regional vessels so that the aorta loses a great deal of its elasticity. These circumstances make it perilous or exceedingly difficult to remove portions of the aorta from adult patients by the techniques which are currently employed. Hence, it is important to emphasize that coarctation of the aorta should be recognized in childhood while the vessels are still elastic and there is still a reasonably good chance for successful correction of the malformation.

Fig. 1. Blood Pressure Chart (Arm) from a Twelve Year Old Boy, Showing Reduction in Hypertension by Surgical Removal of a Coarctation of the Aorta.

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Erythroblastosis Fetalis: Diagnosis and Treatment*

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NO convincing evidence has yet been presented that erythroblastosis fetalis is not fundamentally due to a straightforward immunologic reaction. Therefore, in the majority of cases the diagnosis of this disease is easily made or confirmed by a series of laboratory procedures designed to show this immunologic reaction has taken place. Our diagnostic tests may therefore be divided into four categories:

DIAGNOSIS

I. *We must prove that there is incompatibility* between the bloods of mother and child. Such proof rests, of course, upon our Rh tests. The simplest of these is the demonstration that the mother is Rh negative and the child, Rh positive. Such evidence of incompatibility is usually easily understood and interpreted. But what of the case where the clinician has every reason to suspect erythroblastosis fetalis and the laboratory reports both mother and child to be Rh positive? In such event the clinician is justified in requesting Rh subtyping or studies involving the ABO system. Or what of the very common instance where the mother and baby are both reported as Rh negative, yet the infant is obviously sick? The answer, in this case, usually is that the child is actually Rh positive, that his cells are so saturated with maternal antibody that the laboratory cannot obtain a positive test, and that no one is actually wrong or at fault.

In any case, simple proof of the existence of incompatibility is not diagnostic of erythroblastosis fetalis and in every case it is necessary to undertake further tests.

II. *The second step in diagnosis* is to prove that the mother is sensitized to an antigen not common to her and the baby. This usually involves tests of the maternal serum for Rh antibodies. These tests are now reliable and they are perhaps the most valuable of the whole battery. I should like, however, to point out that they have certain limitations:

1. A positive test for maternal antibodies does not necessarily mean that the baby has or will have erythroblastosis fetalis. Sensitization may have been caused by transfusion or by a previous pregnancy and have no effect upon an Rh negative child. Moreover reports are now accumulating of cases where the mother is sensitized and has had erythroblastotic babies and yet in a later pregnancy gives birth to an Rh positive child who appears to be unaffected by the maternal antibodies.

2. The type of antibody found offers very little indication of the type of disease in the child. It is true that the so-called blocking antibodies are usually associated with the more severe forms of erythroblastosis fetalis and are usually of more serious import. But this is not invariably true and it is not usually possible to predict the type of fetal disease from the type of maternal antibody.

For example: We have followed one mother who has had her third, fourth, and fifth deliveries in the period since it has been possible to distinguish between the two types of Rh antibodies. At the time of the third delivery this woman had a blocking antibody titer of 128. The child was slightly jaundiced and had a mild anemia from which he recovered

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without transfusion. Throughout the fourth pregnancy this mother's Rh blocking antibody titer remained at 128 yet the child had severe icterus gravis and, despite treatment, died of pulmonary hemorrhage on the third day of life. The same antibody titer persisted throughout the fifth gestation which terminated at the seventh month with the delivery of a macerated still-born fetus.

3. The titer of antibody found is not indicative of the type of severity of fetal disease. This statement appears generally in the literature, and it is one upon which workers are agreed. But I should like to go further and say that even a rising maternal titer in pregnancy does not necessarily mean that the baby will have erythroblastosis fetalis. Davidsohn and co-workers of Chicago have undertaken artificial insemination in a number of cases of sensitized mothers. Recently they have carefully followed the titers of these mothers in pregnancy. And in several of the cases, even though the baby was Rh negative and in no way affected, the maternal antibodies showed an anamnestic response with a rise beginning in the fourth month and continuing through the early postpartum period. We in our laboratory have encountered the same type of response. Moreover, severe fetal damage may occur without a rise in maternal titer. The falling titer in our experience has always spelled disaster.

III. *Having shown that incompatibility exists* and that maternal sensitization has occurred, our next step is to show that maternal antibodies have been passively transferred to the fetus. This involves testing the baby's serum for Rh antibodies. In most cases of erythroblastosis fetalis cord serum or serum drawn soon after delivery will be positive for Rh antibodies, and in this event the titer of fetal antibodies appears to be of considerable prognostic significance. By this I mean that the ratio of fetal antibody titer to maternal antibody titer is indicative of severity of disease in the infant, for the more closely this ratio approaches 1.0 the more severe the fetal disease is likely to be. There is again one exception to the rule: Maternal antibodies may be and are passively transferred to the normal Rh negative baby. Therefore, the discovery of Rh antibodies is not significant unless it is also shown that they are specific for the child's cells.

IV. *The fourth, final and probably the most important test* is the proof that maternal antibody has become attached to fetal cells. There are several ways of arriving at this proof, but the simplest is to suspend the cells in 20 per cent or 30 per cent albumin. Cells of affected infants quickly become agglutinated in this medium and this simple test renders the diagnosis almost certain.

To summarize, then, the laboratory diagnosis of erythroblastosis fetalis rests upon demonstration: of fetal-maternal incompatibility; of active maternal sensitization; of passive transfer of maternal antibody to the fetus; and of sensitization of fetal cells.

All of these tests may sound somewhat complicated, but a case illustration will show how simple they may be. The other evening about thirty minutes past 4:00 a young and excited father arrived in the Out Patient Department with an icteric baby. If he had started with any note or message from an obstetrician, he had long since lost or forgotten it. The resident saw immediately that this was probably a case of erythroblastosis fetalis and within five minutes had specimens of blood from the baby and the father in the laboratory. It required about two minutes to determine that both the baby and the father were Group O, Rh positive, and within another five minutes it had been determined that the child's cells would agglutinate in 30 per cent albumin and that his serum agglutinated Rh positive but not Rh negative cells. Therefore, at twenty minutes of five, or at the end of ten minutes, the laboratory had confirmed the clinical diagnosis of erythroblastosis fetalis. And by 5:00 Rh negative blood was cross matched and awaiting the resident's discretion concerning treatment.

TREATMENT

Now for a few comments upon the various methods of treatment: It is impossible to discuss the management of erythroblastosis fetalis without dividing the disease into the four traditional categories, because each of the different forms of the disease is distinct in itself and requires a quite different approach.

Congenital Anemia. The simplest and most easily treated form of erythroblastosis fetalis is the type known as congenital anemia. By this I mean the baby who appears well in the nursery, who is not severely jaundiced, and who may not attract any attention until the tenth or twelfth day of life, or even later. These babies follow a characteristic course. In the first ten days or two weeks of life, the red count falls insidiously and the appetite may gradually fail. Upon physical examination very little is found except an extreme pallor. At postmortem examination the spleen and liver may be somewhat enlarged but this enlargement is not always appreciable during life. If the child is not treated, he may survive, and in a considerable number of cases does survive; if he is treated he responds quickly with a rise in red count and an increase in appetite and in general well-being. However, his red count is unlikely to remain at normal levels even with vigorous transfusion and for the first two or three months of life the bone marrow response is unlikely to meet the infant's demand for hemoglobin. The red counts of some children, therefore, remain at levels of $2\frac{1}{2}$ to $3\frac{1}{2}$ million during this aregenerative phase. Four questions frequently arise in connection with these babies: First, should they be breast fed? The answer is no. The colostrom is as rich in maternal antibodies as is the serum and the breast milk also contains considerable amounts of easily demonstrable antibodies. There is also some evidence to the effect that the infant's intestinal tract, at least during the first two weeks of life, is permeable to these antibodies and the babies, clinically, do badly upon breast feedings. I do not here wish to imply that Rh incompatibility alone is any reason for withholding breast feeding from the child of an Rh negative mother. It is only when the mother is sensitized and the child is Rh positive that it is necessary to remove the baby from the breast. The second question which arises is, how long should these babies be followed in the neonatal period before assuming that their counts will not fall? To the best of our knowledge the answer to this question is approximately 5 to 6 weeks. We have seen a few babies in whose mothers' serums antibodies were demonstrable, but whose counts remained at normal levels until the fifth or sixth week of life and then fell apparently abruptly to 2 or $2\frac{1}{2}$ million. Therefore, the Rh positive child of an Rh negative mother, and particularly of a mother who is known to be sensitized, should be seen at frequent intervals during the first six weeks. The third question which arises is how to manage the baby during the aregenerative phase. On the whole, we have felt that these children do better at home than in hospital, and we bring them back at about ten-day intervals for hemoglobin determinations and red counts. Further transfusion is not undertaken unless one or more of the four following complications occurs:

1. diarrhea
2. failure to gain weight
3. loss of appetite
4. a fall in red count below $2\frac{1}{2}$ million or a fall in hemoglobin below 50%.

The fourth question which has recently arisen in connection with these babies is whether to transfuse them with Rh positive or Rh negative blood. Those who argue in favor of use of Rh positive blood believe that the antibodies passively transferred from the mother will be more quickly eliminated and, therefore, that recovery will be more rapid. Our studies show that this argument has no basis in experimental fact. In the presence of an excess of Rh positive blood we find that Rh antibodies may become dissociated from the antigen and attached to the fresh cells which are added. Moreover, as I have in-

dicated, there are free antibodies in the infant's bloodstream which may quickly become attached to incoming Rh positive cells, and the elimination of sensitized erythrocytes may place an intolerable burden upon the baby. We, therefore, feel that as long as any jaundice persists, or as long as any antibodies exist in the child's serum, the use of Rh positive cells is not indicated. As soon as the jaundice and the antibodies disappear—and they are usually gone by the end of the first month of life—there is no danger in using Rh positive blood.

Icterus Gravis. The second category of the disease and the most difficult to manage is the form traditionally known as icterus gravis. These are the babies who are jaundiced from the very early neonatal period and who quickly attract attention in any newborn nursery. In addition to being jaundiced they are frequently lethargic and upon examination one almost invariably finds a grossly enlarged liver and spleen. These infants are frequently not anemic and their counts may never fall to dangerous levels. They are, however, generally sick. The spleen and liver are choked with massive accumulations of immature red cells and there is some indication that the liver, at least, is otherwise immature. The myocardium may also be affected and these babies sometimes die of heart failure. The central nervous system is also vulnerable, and kernicterus and cerebral hemorrhage, unfortunately, are all-to-frequent complications of the disease. Finally, there is often a considerable degree of atelectasis, and pulmonary hemorrhage or hemorrhagic pneumonia is a frequent cause of death. In other words, these children rarely die of anemia. They most frequently die of pulmonary hemorrhage, or hemorrhagic pneumonia: they often die of kernicterus or cerebral hemorrhage, and they sometimes die in heart failure.

For these babies in the past, transfusion has certainly not been the answer; upon the other hand, not a few babies have died following large transfusions, whether of Rh positive or of Rh negative blood. In the past we have found it advisable to treat these infants very conservatively, keeping them warm, handling them as little as possible, maintaining their fluids with generous amounts of glucose, and making no attempt to keep the hemoglobin and red count at normal levels. Transfusions have been withheld within the first 5 days of life unless the red count has fallen below $3\frac{1}{2}$ million, and when transfusion has been undertaken, it has been limited to 5 cc. per pound. Under this treatment, fortunately, at least 75 per cent of the children have survived. Within the last few months, however, a new treatment has been proposed for this type of case. This is the exchange transfusion which has attracted so much publicity and attention from the layman. Theoretically the exchange transfusion has a place in the treatment of severe icterus gravis, and the Boston group have been successful in treating 16 such cases. There have been 2 deaths. I should like to point out that this treatment is in the experimental stages, and has been reserved for babies who in the opinion of the clinician would not otherwise survive. Therefore, before an exchange transfusion is contemplated, the clinician assures himself that the mother is sensitized, that the baby is Rh positive, that the baby's cells are saturated with maternal antibody, and that the mother's past obstetric history is such as to indicate that the baby's chances of survival are poor. If these criteria are met treatment is instituted in the following manner:

The cord is clamped and severed about 2 inches from the body. It is unnecessary and undesirable to have a longer cord, in which clots and hematomas may form. These, of course, will interfere with treatment and may lead to danger of introducing emboli. The baby is placed in a Hess bed or in a box where the temperature can be adequately maintained. The operator and his assistant who are, of course, scrubbed and have donned rubber gloves and sterile gowns, cleanse the cord and surrounding area with cord alcohol and drape the baby with sterile sheets. The clamp is then removed from the cord with

the assistant holding the cord with a mosquito clamp, the operator locates the umbilical vein and dilates it with an ordinary vein dilator. Welling of blood into the area usually indicates that the vein has been found and suitably opened. The umbilical arteries do not ordinarily give any difficulty during this procedure, and there is little if any oozing from them. Also, very little blood is lost as a rule from the umbilical vein. After the vein has been dilated, a plastic catheter is introduced. In the event the child's blood count is at about a normal level, 35 to 40 cc. of blood are withdrawn. Approximately 65 cc. of Rh negative blood are then introduced through the same catheter. After a wait of one full minute, this is followed by another withdrawal phase of about 40 cc. of blood, and the procedure is repeated until nearly 500 cc. of Rh negative blood have been washed through the child. Specimens are taken for Rh testing at each withdrawal phase. Clotting is prevented at suitable intervals, at the operator's discretion, by addition to the system of about 0.2 cc. of heparin. The treatment ends with addition of a small increment of Rh negative blood. The amount of this increment is, of course, determined by the initial degree of anemia, and usually amounts to about 10 cc. per pound.

The entire procedure requires between 2 and $2\frac{1}{2}$ hours. I should like to emphasize that this operation is undertaken in a leisurely manner. The cord can be used for approximately 6 hours after delivery, and there is usually no indication for haste. Certainly there is every indication to carry out adequate resuscitation measures and to obtain appropriate serologic and hematologic studies before this intricate and dangerous procedure is instituted. After the transfusion is completed, the child is placed upon prophylactic sulfadiazine and penicillin, because of the ever-present danger of infection.

In 15 of the 16 cases successfully treated in this way, the babies have required no further transfusion; there have been no cord infections, and insofar as can be determined, kernicterus has not occurred.

Hydrops. The third form of the disease, fetal hydrops, does not ordinarily yield to treatment, and the babies, of course, are usually stillborn or die within a few minutes. In our experience, only one child has survived this form of the disease. In this case, no attempt was made to control the edema, which persisted for about 2 weeks, and the red count was permitted to remain at about 2 million for the same period of time. This baby is now ten months old; it is mentally competent, and the only residual is a discoloration of the teeth, which are intensely blue.

Intrauterine Death. The fourth form of the disease is intrauterine death, which rarely occurs before the sixth month of gestation. On the face of it, this would appear to be purely an obstetric problem, but it is in part being converted to a pediatric problem through the use of premature induction of labor or premature cesarean section. As yet we have no figures to indicate that this measure is successful in saving the lives of these infants, and we must await the results of further experience before we can make any definite statement as to the value of early delivery. The children so delivered, as a rule, present all the problems of prematurity combined with those of severe icterus gravis. The babies are very difficult to manage, and many of them die on the third day of life with typical signs of kernicterus. In appropriately selected cases exchange transfusions are now being used in combination with early delivery, and the reports thus far have been somewhat encouraging. This whole field, however, presents new problems to the pediatrician, and the results of treatment will depend ultimately upon his clinical judgment and skill.

The Ketosis Problem*

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INTRODUCTION

KETOSIS has long constituted one of the true medical emergencies. In light of the modern knowledge of the underlying pathology, all deaths are preventable, and yet Beardwood, in surveying 1865 diabetic cases in various Philadelphia hospitals, noted 220 with acidosis, of whom 52 died; and, in a five year period at the Philadelphia General Hospital, Dillon and Dyer reported 110 deaths from acidosis. The onus for these deaths can be divided between the general practitioner, who apparently all too often fails to comprehend the significance of acidosis, and organized medicine, which has failed to educate the public properly. That fatalities can be practically eliminated has been demonstrated by Root, who in a recent series of 126 cases had only three deaths. The moaning, restless, dull or semi-stuporous patient, with flushed face, sweet breath, Kussmaul breathing, dry cold skin, rapid pulse and low blood pressure, presents the most important problem in handling Diabetes, not only as to therapy but also as to understanding of the basic physiological fault.

HISTORICAL BACKGROUND

That these changes were due to the formation of ketones, as a result of carbohydrate lack, was recognized in 1895 by Hirschfield, and it has long been an accepted concept that the ketone bodies—acetoacetic acid, beta-hydroxybutyric acid and acetone—represented incomplete oxidation products of the fatty acids, which required concomitant oxidation of the carbohydrate metabolites. This was well expressed by Woodyatt in 1910, who stated, "When the mixture of metabolites oxidizing in the body contain more than three molecules of higher fatty acids to one of glucose, then the body 'smokes' with acidosis compounds, like an automobile smokes with too much oil in the cylinders". The oxidation of all fatty acids was explained by the Knoop hypothesis of successive beta oxidation, which held that fatty acid degradation in the organism occurred by the loss of two carbon atoms at a time, with the initial point of oxidation attack at the Beta or second carbon atom removed from the carboxyl group, and the splitting off of the two carbon atoms, presumably as acetic acid. Finally, one molecule of butyric acid would remain and, in turn, be oxidized to acetoacetic or beta-hydroxybutyric acid. The ketogenic-antiketogenic ratio of Schaffer offered a quantitative explanation of the influence of carbohydrate utilization upon ketone secretion, and explained the accumulation of these noxious substances in Diabetes.

Another less-popularly accepted theory, that attempted to explain some of the fallacies in the above, was Hurtley's multiple alternate oxidation hypothesis, which stated that the long fatty acid molecule was oxidized along the entire length of the chain at alternate carbon atoms. Thus, the fatty acid would disappear completely, being replaced by an equivalent amount of ketone bodies.

PRESENT CONCEPTS OF PATHOLOGICAL PHYSIOLOGY

These were the accepted concepts of the mechanism of ketosis formation until 1940, when Stadie, Zapp and Lukens began their series of experiments with animal livers, studying oxygen utilization, acetic acid formation or rather non-formation, and the balance between fatty acids oxidized and ketones

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formed. Their results refuted the Knoop theory and apparently corroborated the multiple alternate oxidation route. Also, using liver preparations, they demonstrated that ketones could be utilized peripherally. They hypothesized that up to a certain level all fat catabolized was completely oxidized; hence, there would be no ketonuria. Beyond this level, all fat catabolized was not completely oxidized; hence, part of the fat catabolized was excreted unburned in the form of ketone bodies. The action of carbohydrates was simply to spare fat oxidization; there was no molecular reaction, hence there was no molecular ratio between the two. They concluded that, when the demand for fat calories exceeded a certain level, approximately 2.5 g. of fat/ky/day for the resting state, ketone bodies in excess of needs were formed by the liver. The excess was excreted in the urine—if the excessive fat catabolism continued unchecked, ketosis and coma followed.

Further light has recently been cast on the difficult problem by the work of Medes, Weinhouse and Floyd, at the Lankenau Institute, Philadelphia, by means of experiments using heavy carbon isotope tags. They attached a C^{13} tag to a carboxyl group of various fatty acids, traced it through to a two carbon stage and back into two positions in the ketone bodies. This confirmed the recently advanced theory of McKay, termed the Beta oxidation-condensation hypothesis, which stated that, by successive beta oxidation, the fatty acid molecule is split into two-carbon units and reassembled with subsequent random condensation to the ketone bodies. As can be seen by the following diagram, the inconsistencies of the classical beta-oxidation become apparent and the possibility of multiple alternate oxidation, as previously mentioned, is precluded.

Theories of Ketone Body Formation

B-Oxidation

$$C{-}C{-}C{-}C\div C{-}C\div C{-}C^{13}OOH$$
$$\downarrow$$
$$CH_3COCH_2COOH$$

Multiple Alternate Oxidation Theory

$$C{-}C{-}C{-}C\div C{-}C{-}C{-}C^{13}OOH$$
$$\downarrow \qquad\qquad \downarrow$$
$$CH_3COCH_2COOH \quad CH_3COCH_2C^{13}OOH$$

B-Oxidation-Condensation Theory

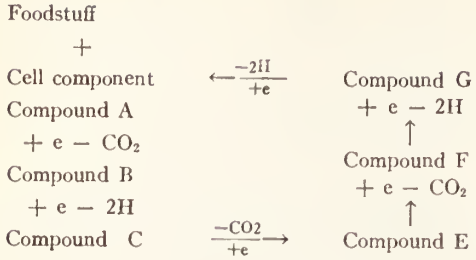
$$C{-}C\div C{-}C\div C{-}C\div C{-}C^{13}OOH$$
$$\downarrow \quad \downarrow \quad \downarrow \quad \downarrow$$
$$CH_3COOH \; CH_2COOH \; CH_2COOH \; CH_2C^{13}OOH$$
$$\downarrow$$
$$CH_3C^{13}OCH_2C^{13}OOH$$

Carrying their work with isotopes still further, Medes and others have been able to demonstrate that ketone bodies are actually formed and utilized in various organs of the body, although so transiently, that they can not be demonstrated by any other method. It had previously been recognized that fat could be completely oxidized in the muscles themselves, but this constituted the first actual evidence of ketone body formation outside of the liver.

UTILIZATION OF KETONES

Although it was as long ago as 1914 that Marriot suggested that ketone bodies might be utilized, only recently, following the work of Drury, of Stadie, and following these present isotope experiments, has this concept been accepted and understood. Hence, a revolutionary change in the realization of the significance of ketosis has transpired. The above findings confirm other recent experiments that seem to eliminate the distinctions that exist between carbohydrate, protein and lipid classifications inasmuch as many of their intermediary metabolities are common to all three classes of foodstuffs. It appears that pyruvate, acetoacetate, and acetate are all metabolized by a common pathway, becoming oxidized by Krebs' tricorboxylic acid cycle, which functions as a catalyst requiring only a minimal amount of simple carbohydrate to work properly. A total diabetic would be unable to metabolize even ketones, unless the catalytic cycle was initiated by some simple carbohydrate, such as citric acid, or other substance below the site of block in the carbohydrate chain.

Oxidation of Foodstuffs



So, at long last, the ketone bodies appear in their true light. They are readily usable sources of energy similar in nature and ultimate disposition to carbohydrate metabolites. They require some carbohydrate as a catalyst, but the old ketogenic-antiketogenic ratio no longer holds. They possess no specific toxicity but are relatively strong acids, capable of upsetting the acid-base balance and tying up carbonic acid.

CLINICAL APPLICATION

Of what practical import is this revised viewpoint on ketosis? To return to the restless, semi-comatose, diabetic patient, it is now apparent that his comatose state is not the result of absorption of noxious ketone bodies, but rather the result of dehydration. The cold, dry skin, rapid pulse, and circulatory failure can also be ascribed to the dehydration which is a result of the prolonged glycosuria and ketonuria, with resulting diuresis and the loss of electrolytes. The air-hunger represents an attempt of the body to compensate for the reduced plasma CO_2. The abdominal cramps result, not only from dehydration, but also from depletion of chlorides, which are swept out into the urine along with Sodium. Whether the blood sugar level should happen to be high or relatively low does not indicate the severity of the ketosis or affect to any extent the basic therapeutic program. Therefore, next to the all important administration of insulin to correct the original metabolic defect, the vigorous correction of the dehydration would appear imperative. In view of the foregoing discussion, it seems this best could be done with large amounts of water and Sodium Chloride. To use bicarbonate would be merely treating a symptom and while perhaps affording a temporary relief, would only excite the body toward further acid formation. Lactate solution as recommended by Hartmann is readily sterilized, stable, and can be given intravenously or by hypoclysis, but its action is essentially that of sodium bicarbonate. It would seem physiologically sound to add some simple metabolite, such as citric acid or citrate which is in equilibrium with components of the tricarboxylic acid cycle and hence might stimulate ketone utilization.

SUMMARY

(1) Ketosis continues to account for a large number of diabetic deaths.

(2) Ketone bodies are formed according to the Beta-oxidation-condensation hypothesis of McKay.

(3) They are formed, not only in the liver, but in other organs of the body.

(4) Ketones are, in fact, merely potential fuel, requiring a small amount of carbohydrate as a catalyst for their proper utilization.

(5) Treatment should consist fundamentally of the extensive use of insulin and large amounts of Sodium Chloride and water.

Transactions of the Sections

SECTION ON GENERAL MEDICINE

January 27, 1947

Diffuse Calcification of the Pancreas: a Form of Chronic Pancreatitis. C. Wilmer Wirts, jr, M.D. (Commentator: Russell S. Boles, M.D.) (*Abstract 1, below*)

The Pharmacologic Restoration of Gastric Motility and the Promotion of Evacuation of the Stomach after Section of the Vagus Nerves for Peptic Ulcer. Thomas E. Machella, M.D. (Commentator: Henry L. Bockus, M.D.) (Printed in the *Transactions & Studies*, vol. 15, no. 1, April, 1947.)

The Treatment of Peptic Ulcer, with Special Reference to Vagotomy. Julian M. Ruffin*, M.D. (Printed in the *Transactions & Studies*, vol. 15, no. 1, April, 1947.)

February 24, 1947

Periodic Diseases. Hobart A. Reimann, M.D. (Commentator: William G. Leaman, jr, M.D.) (No abstract submitted.)

Chronic Pulmonary Coccidiomycosis. Harold L. Israel*, M.D. (Commentator: David A. Cooper, M.D.) (*Abstract 2, below*)

The Study of Pulmonary Function in Clinical Medicine. André Cournand*, M.D. (No abstract submitted.)

March 24, 1947

The Ketosis Problem. Henry F. Page*, M.D. (Commentator: Garfield G. Duncan, M.D.) (Printed in this issue of the *Transactions & Studies*.)

The Treatment of Diabetic Gangrene with Intravenous Diethyl Oxide. Edward S. Dillon, M.D. and Carl S. Nadler*, M.D. (Commentator: David W. Kramer*, M.D.) (No abstract submitted.)

The Control of Diabetes and the Treatment of its Complications. Howard F. Root*, M.D. (*Abstract 3, below.*)

* By invitation.

April 28, 1947

The Importance of Inhalant Allergens in Atopic Dermatitis. Louis Tuft, M.D. (Commentator: Carroll S. Wright, M.D.) (No abstract submitted.)

Treatment of Plant Dermatitis with Simple Alcoholic Extracts. Samuel E. Rynes, M.D. (Commentator: Harry L. Rogers, M.D.) (No abstract submitted.)

The Treatment of Infectious Asthma and Asthmatic Bronchitis with Penicillin in Beeswax and Oil: a Preliminary Report. Leslie N. Gay*, M.D. (To be published in the next issue.)

SECTION ON OPHTHALMOLOGY[1]

January 16, 1947

The Use of Beta Radiation in Ophthalmology. Albert D. Ruedemann*, M.D. (Commentator: Eugene P. Pendergrass**, M.D.)

February 20, 1947

Syndrome of Paroxysmal Lacrimation When Eating, Associated with Homolateral External Rectus Paralysis. Frank C. Lutman*, MC, AUS. (Commentator: Robert A. Groff**, M.D.)

The Syndrome of Sphenoidal Ridge Meningioma. Robert H. Trueman*, M.D. (Commentator: Robert A. Groff**, M.D.)

The Protection and Maintenance of Night Vision for Military Personnel. Robert Peckham*, PH.D.

March 20, 1947

Factors Operative in Resorption from the Vitreous. Ludwig von Sallmann*, M.D.

[1] The presentations at this Section are customarily abstracted in the *American Journal of Ophthalmology* and the *Archives of Ophthalmology*.

** Fellow of the College, but not a member of the Section.

April 24, 1947

Rubeosis Iridis: Case Report. Joseph Waldman, M.D., and David Naidoff*, M.D.

Contaminated Ophthalmic Ointments. Louis Lehrfeld, M.D., and Edward J. Donnelly, M.D. (Commentator: Louis Gershenfeld*, D. Sc.)

Vitreous Infections and Streptomycin: Experimental Studies. Irving H. Leopold, M.D., Richard Dennis*, M.D., and Marjorie Wiley*, B.A.

The Role of the Vertically Acting Muscles in Concomitant Strabismus. Edmund B. Spaeth, M.D. (Commentator: Glen G. Gibson, M.D.)

SECTION ON OTOLARYNGOLOGY[2]

February 19, 1947

Cyst Involving Frontal Sinus. Austin T. Smith, M.D., and James T. Spencer, Jr, M.D.

Labyrinth Reactions, Before, During, and After Streptomycin Therapy. Julius Winston*, M.D. (Commentator: F. H. Lewey*, M.D.)

The Drum Membrane and the Tympanic Antrum. O. V. Batson, M.D.

April 16, 1947

Diagnosis and Treatment of Hydrops of the Labyrinth. Kenneth M. Day*, M.D.

SECTION ON PUBLIC HEALTH, PREVENTIVE AND INDUSTRIAL MEDICINE

April 7, 1947

The Present Status of the Pennsylvania Hospital Survey and its Implications. Hubley R. Owen, M.D.

The Present Status of Chest X-ray Surveys in Philadelphia. Martin J. Sokoloff, M.D.

Public Health and the Health of the Public. William Harvey Perkins, M.D.

Abstracts

Abstract 1

Diffuse Calcification of the Pancreas: a Form of Chronic Pancreatitis.

C. Wilmer Wirts, jr, M.D.

Reports dealing with chronic pancreatitis are not common in the American literature. This is probably due more to the difficulty of diagnosis and the lack of a satisfactory confirmatory test than to the low incidence of the disease. During the past year we have observed four patients at Jefferson Hospital with chronic pancreatitis associated with diffuse calcification of the pancreas. The rather striking clinical course in these patients and the paucity of literature dealing with this subject stimulated us to make this report. At the time the data was accumulated only 20 similar cases were found described in the literature and these were listed under a variety of titles, such as disseminated calcification of the pancreas, pancreatitis petrificans and diffuse parenchymal calcification of the pancreas. The etiology is unknown although the symptoms suggest it is due to recurrent attacks of acute pancreatitis. The pathology noted histologically shows pronounced inter- and intralobular fibrosis with minute calculi filling the smaller ducts and acini of the pancreas.

The outstanding symptom of which these patients complain is some form of abdominal pain, usually existing for months or years. Steatorrhea and creatorrhea are present in about twenty-five per cent of the patients and in the twenty-four cases reported (including the four referred to in this report), eight had transient jaundice with enlargement of the liver; three had diabetes; in nine cases a history of excessive indulgence in alcohol was obtained; three patients had an associated pulmonary tuberculosis and three had syphilis.

[2] The presentations at this Section are customarily abstracted in the *Archives of Otolaryngology*. Meetings in January and March were held jointly with the Philadelphia Laryngological Society, as were the meetings listed above; only the programs arranged by the Section are recorded here.

In any patient with a long history of upper abdominal pain the possibility of disseminated calcification of the pancreas should be considered. Subsequent confirmation of the diagnosis is then dependent upon (1) plane film of the abdomen including that area between the first and fourth lumbar vertebrae; (2) stool examination for total fat and creatorrhea and (3) pancreatic function test (Secretin test).

Acute phases of this condition must be treated symptomatically but when it is far advanced and a true pancreatic insufficiency established, a low fat, high caloric diet, vitamins and large doses of pancreatin may be of help. Recently partial and total pancreatectomies have been performed in selected patients with intolerable pain and threatened morphinism.

Conclusion: Probably one of the greatest benefits that will accrue from the proper recognition of this disease is that it may prevent the needless removal of a gall-bladder, appendix or kidney. As has been demonstrated in one of our patients the erroneous removal of his gall-bladder led to a series of operations to overcome the sequels of the first, without in the least benefitting the conditions giving rise to the initial symptoms. On one occasion, due to the persistent complaint of abdominal pain for which no organic cause could be found, this patient was also diagnosed as a psychoneurotic. That this error has occurred previously is indicated by the paper of Yaskin, who reported four cases of pancreatic disease in whom a diagnosis of functional disturbance was made. Remaining alert to the possibility of the existence of disseminated calcification of the pancreas in a patient is probably the most important single factor in its recognition.

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Abstract 2

Chronic Pulmonary Coccidiomycosis. Harold L. Israel, M.D.

Coccidiomycosis has been recognized only in the past five years to be more than a local California problem. Infection is readily acquired in large areas of the American Southwest. Infection is manifested in a quarter of cases by clinical symptoms, of which a transient pneumonia and erythema nodosum are the most common. The primary infection occasionally progresses directly to disseminated coccidiomycosis, or coccidioidal granuloma.

There has been until very recently insufficient recognition of the frequency of chronic pulmonary residuals. These appear roentgenologically as "soft" nodules or as thin walled cavities, usually single but occasionally multiple. Respiratory and constitutional symptoms are absent, except for an occasional case characterized by recurrent hemoptysis. Limited necropsy studies suggest that the coccidioidal spherules present in these residuals are usually not viable, and clinically the lesions have been regarded as benign. Recent reports of late dissemination and local granulomatous invasion suggest that the ultimate prognosis may be more serious than anticipated. The clinical simulation of tuberculosis by coccidiomycosis emphasizes the need for investigation of the latter possibility in patients with history of even brief residence in the Southwest whose clinical or roentgenological findings suggest tuberculosis, in any of its varied forms: pulmonary, osseous, meningeal, pleural, pericordial, adrenal, etc.

Abstract 3

The Control of Diabetes and the Treatment of its Complications. Howard R. Root, M.D.

The magnitude of the diabetic problem impresses physicians today more than ever, not only because diabetes has risen from 27th to

8th place in the United States in mortality tables, but complications of diabetes with their effects upon vision, upon the legs and upon the heart are increasing greatly the problems of invalidism. Experimental demonstrations of the various causes for diabetes have been increased by the demonstration that persistent hyperglycemia produced by Lukens in normal cats will finally produce destruction of the Islands of Langerhans and diabetes. This cannot help but influence methods of treatment. The Cori demonstration of the relation between insulin and anterior pituitary substance in the carbohydrate cycle may lead to other even more important discoveries just as the use of radioactive isotopes is introducing new ideas in carbohydrate metabolism. The importance of diabetes in producing renal lesions and hypertension is further demonstrated.

In the treatment of diabetes, early diagnosis is to be stressed and the value of surveys in whole communities is being demonstrated. The early use of insulin and the continued control of diabetes by means of diet and insulin are urgently needed if the onset of the malignant complications of diabetes is to be postponed. Insulin mixtures are in common use. The frequency and severity of the complications in the feet of diabetic patients is increasing generally. Some provision will be necessary for the long continued care of patients who present many sided vascular complications of diabetes.

Pathological Society of Philadelphia

Proceedings of the Meetings, February–May, 1947

Meeting, February 13, 1947

Nesidioblastoma. A. Reynolds Crane, m.d. (*Abstract 1, below.*)

The Use of Lecithin to Differentiate between True and False Hemagglutination. William P. Belk, m.d., and Margaret K. Wilson. (*Abstract 2, below.*)

Applications of Blood Volume Measurements. Max M. Strumia, m.d., Alton D. Blake, jr, m.d., Maurice Nance, m.d., Isaac Sharpless, m.d., and Gilman Heggestad, m.d. (No abstract supplied.)

Meeting, March 13, 1947

Similarities of Lesions Induced by Lack of the Anti-stiffness Factor, Hypervitaminosis D, and Human Calcinosis. John Lansbury, m.d. (No abstract supplied.)

The Leukocytosis-promoting Factor of Inflammatory Exudates. Valy Menkin, m.d. (*Abstract 3, below.*)

A Routine Method for the Rapid Determination of Susceptibility to Penicillin and Other Antibiotics. Amedeo Bondi, jr, ph.d. (*Abstract 4, below.*)

Meeting April 17, 1947

The Anatomical Basis of the Autonomy of the Renal Circulation. Norbert Goormaghtigh, m.d. (Professor of Pathology, University of Ghent, Belgium). (No abstract supplied.)

Meeting, May 8, 1947

Pulmonary Adenomatosis Resembling Jagsiekte in a Guinea Pig. Robert F. Norris, m.d. (*Abstract 5, below.*)

Pulmonary Adenomatosis in a Human. A. Reynolds Crane, m.d. (*Abstract 6, below.*)

Hodgkin's Disease: Its Relation to the Other Neoplasms of Lymphatic Tissue. R. Philip Custer, m.d., and William G. Bernhard, m.d. (*Abstract 7, below.*)

Abstract from Meeting, November 19, 1946

The Pathology of Infectious Mononucleosis. R. Philip Custer, m.d., and Edward B. Smith, m.d. (*Abstract 8, below.*)

Abstracts

Abstract 1

Nesidioblastoma. A. Reynolds Crane, m.d.

Tumors composed of pancreatic islet cells were recognized as early as 1902, but their clinical significance was not established until 1927. These tumors occur equally in both sexes and most frequently in middle life (30–50). Clinically, the patients present a triad of 1.) symptoms of nervousness, pallor, sweating, convulsions, confusion and coma, 2.) hypoglycemia and 3.) prompt recovery on the administration of glucose. The five hour glucose tolerance test shows a prolonged curve of the diabetic type without recovery from the late hypoglycemic phase.

Surgical exploration should be done following diagnosis. The lesions are located in all portions of the pancreas, may also be extrapancreatic and are frequently multiple. The size varies from 0.1 cm. to 15 cm. in diameter, but all cases with clinical symptoms have been greater than 1 cm. in diameter. The lesions have been shown to contain much more insulin per gram of tissue, than normal pancreas. They are firm and red in contrast to the yellow pancreas and are partially or completely encapsulated. The component cells are similar

to the alpha and beta cells of normal islets and the specific granules of both cell types have been repeatedly demonstrated. A ductile pattern is common, for these tumors are derived from pancreatic duct epithelium. Varying degrees of fibrosis and hyalinization occur. Mitoses are often present. Thirteen malignant cases have been reported and many have been suspected of being malignant. The fate of this latter group will be most important in ultimately establishing criteria for recognition of the malignant forms.

Abstract 2

THE USE OF LECITHIN TO DIFFERENTIATE TRUE AND FALSE HEMAGGLUTINATION. William P. Belk, M.D., and Margaret K. Wilson.

A suspension of lecithin has the property of dispersing red cell aggregates of pseudo-agglutination, that is, those produced by the rouleau forming property, but not those of true agglutination. This was demonstrated some years ago by Lattis.

The authors applied lecithin to titrations of isoagglutinins and observed moderate reduction in titre in 14 instances and no reduction in 7. In no instance, however, was agglutination completely inhibited, but was always strongly marked in the higher serum concentrations. Long practical use of this method for differentiating between true and false hemagglutination has in no observed instance led to error.

This practice is recommended as valuable and, apparently safe, in the selection of blood for transfusion whenever aggregates of doubtful nature appear.

Abstract 3

THE LEUKOCYTOSIS-PROMOTING FACTOR OF EXUDATES. Valy Menkin, M.D.

The earlier studies of the writer have demonstrated the presence of a leukocytosis-promoting factor (LPF) in inflammatory exudates capable of reasonably explaining the mechanism of leukocytosis with inflammation. The factor is present in human exudates. The canine material is both active and innocuous when injected intravenously in human beings. This suggests the clinical application of this factor. As extracted, it is associated with the pseudoglobulin fraction of exudates, and it is very soluble in an aqueous medium. After several months the material, even though left in a dessicator *in vacuo* under phosphoric anhydride, gradually becomes insoluble, and this insoluble material tends to be relatively inactive. However, if the saline suspension of the material is centrifuged, the supernatant fluid is found to contain the active LPF. The fluid unless concentrated by evaporating is Biuret negative, and it is heat stable. The fluid can be evaporated to dryness on a steam bath, and then the newly obtained dried material is found to be also insoluble. Yet a suspension of this newly obtained material is potent in dogs. Tryptic digestion of fresh LPF fails as a rule to inactivate the factor. Boiling the freshly obtained LPF for 30 minutes inactivates it, but boiling for 30 minutes the dried supernatant fraction obtained from the insoluble aged LPF, which is now presumably denatured, fails to inactivate the potency of the material. Finally, a few measurements on the amino acid nitrogen before and after hydrolysis of the active supernatant fluid from aged LPF indicates that the active principle is a relatively simple polypeptide, presumably attached to the pseudoglobulin when recovered in the fresh state.

Abstract 4

A ROUTINE METHOD FOR THE RAPID DETERMINATION OF SUSCEPTIBILITY TO PENICILLIN AND OTHER ANTIBIOTICS. Amedeo Bondi, jr, M.D.

To be of practical value for routine use, a method of testing sensitivity to the antibiotics must be simple and rapid. The disc test described here achieves both purposes. Blood plates are streaked with clinical specimens in the routine fashion for aerobic and anaerobic incubation. Small sterile filter paper discs saturated with antibiotic solutions to be tested are placed on each plate immediately after

inoculation. Following over-night incubation susceptibility of the organisms on the plate is determined by measurement of zones of growth inhibition surrounding the discs. One can readily determine within 24 hours the relative susceptibility of a number of organisms in a mixed culture. Furthermore, as many as three different antibiotics may be compared simultaneously.

The discs, measuring 6.5 mm., are punched from Whatman No. 2 filter paper. These are dipped into solutions to be tested by means of small sterile forceps. The solution of penicillin contains 15.0 units per ml.; the streptomycin solution contains 500 micrograms per ml. The discs, one for each agent to be tested, are placed beside each other on the plate about 20 mm. apart where the maximum growth is likely to occur. Organisms are reported as "very susceptible," "moderately susceptible," and "resistant," depending upon the size of the zones of inhibition.

Such a test may be carried on in any diagnostic laboratory. It is designed as a routine test and as a guide in therapy. The broad limits of susceptibility by this method are believed to be sufficiently accurate for this purpose.

Abstract 5

PULMONARY ADENOMATOSIS RESEMBLING JAAGSIEKTE IN A GUINEA-PIG. Robert F. Norris, M.D.

Adenomatous lesions involving one lung of a guinea-pig were described. The epithelial proliferation appeared to arise in the smaller bronchi. The neighboring alveoli were lined by single layers of columnar epithelium with clear cytoplasm and only slightly hyperchromatic nuclei. Many of these cells contained collections of dark granules which stained less distinctly with Giesma or phloxine and methylene blue than with hematoxylin and eosin. The adenomatous lesions were not thought to be malignant since the walls of the alveolar septa were preserved and metastasis was not observed. The lesions resembled those of jaagsiekte in sheep but the identity of the two diseases was not otherwise established. Although the guinea-pig was inoculated with pleural fluid from a patient convalescing from lobar pneumonia, there was no evidence that the patient suffered from a similar disease.

Abstract 6

PULMONARY ADENOMATOSIS. A. Reynolds Crane, M.D.

This uncommon lesion is the development of a papillary lining of columnar mucous cells in alveoli in multicentric foci throughout the lungs.

A 37-year-old white male was admitted to the Pennsylvania Hospital with cough and intermittent bouts of fever for two years. X-rays showed one lesion in the left lower lobe and two in the right lower lobe. Ultimately an empyema developed and was aspirated. In this fluid were mucous cells in glandular and papillary arrangement. A lobectomy was done, chiefly for symptomatic relief, but with the possibility in mind of eventually attempting to remove other involved portions of lung. The lung grossly showed grey-yellow consolidation of the central third. Histologically groups of alveoli were lined by mucous cells in papillary arrangement. Mitoses were absent, which is also a characteristic of these lesions. There was invasion of the pleura by these cells, but pulmonary lymph nodes showed no tumor.

This type of lesion is interesting from three aspects. First, in relation to the existence of alveolar epithelium, since some lesions appear to start in the peripheral portions of the alveoli. Secondly, in relation to the so-called alveolar carcinomas of the lung, of which it probably represents an early or benign type of lesion. And finally, in relation to an epidemic disease of sheep known as jaagsiekte, and productive of similar lung changes. Similar lesions occur in other animals: horses, guinea pigs and mice. Despite the epidemic nature of the lesion in sheep no etiological agent has been demonstrated. Attempts at virus isolation have failed, and our own attempts in chick embryos and mice have been unsuccess-

ful to date, although the studies are still in progress.

Abstract 7

HODGKIN'S DISEASE: ITS RELATION TO THE OTHER NEOPLASMS OF LYMPHATIC TISSUE.* R. Philip Custer, M.D. and William G. Bernhard, M.D.

The cellular structure of lymphatic tumors is extremely labile, and the transition from one apparently distinct type to another is frequently observed. This was recognized as early as 1906, but has been given credence in relatively few papers since. We have for some years been aware of this fluidity of type that exists in tumors of lymphatic tissues, acutely so after having reviewed the large mass of material submitted to the Army Institute of Pathology during the war years, many of the cases having included from one to three biopsies in addition to autopsies. All cases were accessioned by the Lymphatic Tumor Registry of the American Registry of Pathology, and a considerable number had been reviewed by the consultants of the Lymphatic Tumor Registry.

Any case in which the diagnosis of Hodgkin's disease was not completely acceptable on the basis of either biopsy or autopsy specimens was discarded. The final study material comprised 200 cases in which an autopsy had been performed, and 500 cases in which only biopsies were available. In the autopsy group one biopsy had been performed in 113 cases, two in 21, and three in 4 cases. The biopsy series comprised one sample in 431 instances, two in 60, and three in 9. The serial biopsies served to augment the biopsy-autopsy material in the study of transitions from one variant to another, while the single biopsies proved valuable in determining the incidence of several histologic patterns in the same lymph node.

In addition, there were over 600 cases in which the major diagnosis was lymphosarcoma, reticulum cell sarcoma, lymphatic leukemia, monocytic leukemia, or follicular lymphoblastoma. This group included cases displaying transitions and combinations apart from Hodgkin's disease, and furnished data for completion of the scheme of interrelationship of the lymphomas (Table 5).

With respect to Hodgkin's disease we grouped our cases according to the histologic classification of Jackson and Parker[1] (Hodgkin's paragranuloma, Hodgkin's granuloma, Hodgkin's sarcoma) in deference to the predominating microscopic appearances (Table 1), even though the picture was a mixed one in many instances. We did not find any fundamental difference between Hodgkin's sarcoma and reticulum cell sarcoma, each showing variants from undifferentiated syncytial tumor to well differentiated reticulum cells, and consequently classified these tumors together, irrespective of the fortuitous occurrence of tumor giant cells that could be regarded as Reed-Sternberg cells.

TABLE 1

CASES GROUPED ACCORDING TO THE JACKSON-PARKER HISTOLOGIC CLASSIFICATION

	Autopsy Series	Biopsy Series
Hodgkin's paragranuloma	7	93
Hodgkin's granuloma	120	378
Hodgkin's sarcoma	73	29
Number of cases	200	500

Within the Hodgkin's disease group proper the transitions and combinations observed are shown in Tables 2, 3 and 4. The scheme presented in Table 5 takes into consideration the associated lymphatic tumors. The heavy lines indicate the interrelations most frequently observed in our series, the lighter lines the more uncommon ones; we did not have an instance of change from follicular lymphoblastoma to

* The William Royal Stokes Memorial Lecture on Pathology of the Medical and Chirurgical Faculty of the State of Maryland (22 April 1947), Baltimore, Md., and presented again before the Pathological Society of Philadelphia on 8 May 1947.

[1] This offered a medium whereby we could indicate changes in the histologic pattern within the single category of Hodgkin's disease.

monocytic leukemia, but this possibility is indicated by a dotted line. In addition we found in a few cases associated tumor foci which were indistinguishable from fibrosarcoma.

TABLE 2

TRANSITIONS AND COMBINATIONS OF HISTOLOGIC TYPES

	WITH TRANSITION		WITHOUT TRANSITION		PURE TYPE		COMBINED TYPES		
	NO.	%	NO.	%	NO.	%	NO.		CASES
Autopsy Series (200 cases)									
With Biopsy	54	39	84	61	26	19	112	81	138
Without Biopsy	—	—	—	—	45	74	17	26	62
Biopsy Series (500 cases)									
Sequential Biopsies	21	31	48	69	16	23	53	77	69
Single Biopsy	—	—	—	—	305	71	126	29	431

TABLE 3

TYPE LESIONS OBSERVED IN DIFFERENT LYMPH NODES OR ORGANS OF THE SAME INDIVIDUAL AT AUTOPSY

(129 cases)

Hodgkin's paragranuloma		x	x			x	x	x			
Hodgkin's granuloma	x	x	x	x	x				x		
Hodgkin's sarcoma	x		x	x	x	x	x	x	x	x	
Lymphosarcoma					x	x					
Fibrosarcoma				x							
Follicular lymphoblastoma								x	x	x	
Number of cases	90	13	13	4	3	2	1	1	1	1	

COMBINATIONS OF TYPE LESIONS* OBSERVED IN SINGLE LYMPH NODES

(255 cases)

Hodgkin's paragranuloma		x	x	x				x		x		
Hodgkin's granuloma	x	x			x	x	x	x	x		x	
Hodgkin's sarcoma	x			x			x	x	x	x		x
Lymphosarcoma					x				x			
Fibrosarcoma						x	x					
Follicular lymphoblastoma			x							x	x	x
Number of cases	132	101	7	4	2	2	2	1	1	1	1	1

* Histologic patterns of significantly large fields which, if viewed alone, would justify the diagnoses as listed.

CONCLUSIONS

1) Instead of there being 5 or more separate and distinct neoplasms of lymphoid tissue there is *one*.

2) This single tumor entity may adopt any one of at least 7 different histologic patterns.

3) These may occur singly or in combination in a given patient, or there may be a distinct transition from one type to another during the course of the patients' disease.

4) Two of these variants, Hodgkin's paragranuloma and Hodgkin's granuloma, are clearly inflammatory in nature, yet each may adopt the cellular characters and clinical behaviour of a malignant tumor.

5) It is our impression that this malignant lymphoma (to use an all-encompassing term for the group of variants) is a virus-induced tumor.

TABLE 4

VARIETIES OF MAJOR TRANSITIONS OBSERVED

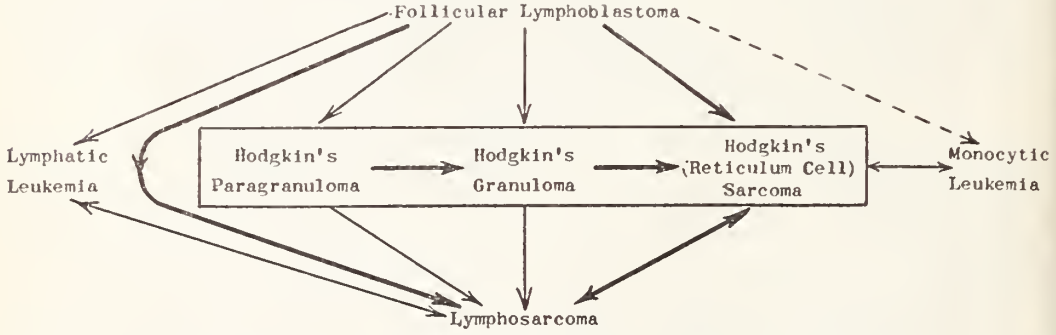
	INITIAL TYPE	TERMINAL TYPE	CASES
Autopsy Series with Biopsy:	Hodgkin's paragranuloma	Hodgkin's granuloma	7
	Hodgkin's paragranuloma	Hodgkin's sarcoma	6
	Hodgkin's granuloma	Hodgkin's sarcoma	28
	Hodgkin's granuloma	Fibrosarcoma	1
	Hodgkin's sarcoma	Hodgkin's paragranuloma	2 (?)*
	Hodgkin's sarcoma	Hodgkin's granuloma	8 (?)*
	Follicular lymphoblastoma	Hodgkin's granuloma	1
	Follicular lymphoblastoma	Hodgkin's sarcoma	1
Sequential Biopsy Series:	Hodgkin's paragranuloma	Hodgkin's granuloma	7
	Hodgkin's granuloma	Hodgkin's paragranuloma	1 (?)*
	Hodgkin's granuloma	Hodgkin's sarcoma	9
	Hodgkin's sarcoma	Hodgkin's granuloma	2 (?)*
	Follicular lymphoblastoma	Hodgkin's paragranuloma	1
	Follicular lymphoblastoma	Hodgkin's sarcoma	1

* It is not clear whether these cases show a reverse transition toward better differentiation, or whether the biopsy merely disclosed a local variant of the major type of lesion observed at autopsy.

† One of these was a combination of Hodgkin's (reticulum cell) sarcoma and lymphosarcoma, the two types being distinct in separate foci.

TABLE 5

INTERRELATIONSHIP OF HODGKIN'S DISEASE AND ALLIED LYMPHOMAS



This diagram represents transitions actually observed between the several variants of malignant lymphoma, and is not to be construed as indicating genetic sequences. The dotted line implies a possible change not yet seen.

Work is already in progress in our laboratories to investigate the disease from this angle.

Abstract 8

(from meeting, November 19, 1946)

THE PATHOLOGY OF INFECTIOUS MONONUCLEOSIS. R. Philip Custer, M.D., and Edward B. Smith, M.D.

This pathologic study was based on the following material, most of which was observed at the Army Institute of Pathology in Washington:

Autopsies	9
Lymph node biopsies	100
Bone marrow aspirates	Many
Bone marrow biopsies	2
Extirpated ruptured spleens	3
Tonsillar "tumor"	1
Liver biopsy	1
Skin biopsies	2

Causes of death in the fatal cases were as follows:

"Spontaneous" rupture of the spleen	4 cases*
Guillain-Barré syndrome	2 cases
Naso-pharyngeal hemorrhage	1 case
Laryngeal edema	1 case
Airplane accident (convalescent case)	1 case

The gross changes were almost exclusively confined to enlargement of lymphoid tissues, especially the spleen which weighed between 400 and 600 gm. in each case. Naso-pharyngeal lymphoid hyperplasia was constant, and in one patient a rapid tonsillar growth suggested tumor. Other tissues presented no significant gross features related to the primary disease except for an occasional cutaneous rash and infrequent icterus.

Histologic observations revealed more or less generalized lesions resembling those of certain known virus diseases, notably perivascular aggregates of normal and abnormal lymphocytes. This type reaction inconstantly involved all tissues studied except the bone marrow; here lymphocytes were absent in sections, but were present in aspirated marrow because of dilution with peripheral blood.

More specific changes were invariably noted in lymphoid tissues. The abnormal lymphocyte characteristic of the disease could be identified in thin, lightly stained sections. *Lymph node* reactions varied from a predominantly follicular hyperplasia to a blurred pattern simulating lymphoblastoma; the latter was due to a lymphocytic and reticulo-endothelial proliferation in the medullary cords. The *spleen* displayed a lymphocytic "infiltration" in the thinned capsule and trabeculae, frequently dissolving the latter and rendering the organ liable to rupture. The pattern was partially effaced in most instances and the follicles widely spaced. Blood sinuses contained considerable numbers of normal and abnormal lymphocytes, and accumulations of these cells constantly cuffed intratrabecular arteries and lay beneath the intima of veins. *Tonsils* displayed ulceration and extensive necrosis in several cases, and the lymphocytic proliferation closely resembled tumor in the tonsil that enlarged rapidly.

A pneumonic exudate in one case was almost exclusively of round cell type, while in another the pneumonia was the usual lobular type with a neutrophil exudate. Small myocardial "infiltrates" which we noted probably explain the electrocardiographic changes described in infectious mononucleosis. Other findings of particular interest were the periportal lymphoid collars in the liver which sometimes attained the proportions seen in leukemia, and the presence of meningo-encephalitis in 4 of the 6 brains examined. The two cases of Guillain-Barré syndrome displayed pronounced peripheral neuritis.

We believe that the majority of cells in the lymphocytic "infiltrates" of connective tissues and perivascular collars are metaplastic rather than inwanderings, i.e., that they are formed in situ and stem from cells of the reticulo-endothelial system.

* Immediate causes of death in these 4 cases were hemorrhage (2), postoperative pulmonary embolism (1), blood transfusion reaction (1). In 3 other cases the ruptured spleen was removed and the patients recovered.

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Changes in Membership

New Members

	Date of Election		*Date of Election*
Simkins, Samuel	2-11-'43	Pietrolungo, Anthony L.	5-10-'45
Corrigan, Patrick H.	4-8-'43	Ziegler, Edwin	10-10-'45
Stasney, Joseph	4-8-'43	Snyder, Joseph	10-10-'45
Peale, Augustin R.	11-11-'43	Wurtz, John W.	11-8-'45
Frank, Jesse H.	11-11-'43	Sheldon, Warner F.	11-8-'45
Scaricaciottoli, Thomas H.	11-11-'43	Mertens, Elizabeth	12-13-'45
McGrew, Donald	11-11-'43	Lawry, Lee	1-10-'46
Foldes, Julius	4-13-'44	Rathmell, Thomas K.	4-11-'46
Brown, Harry E.	11-9-'44	Jenny, Florence B.	10-10-'46
Draper, Harry	12-14-'44	Crane, A. Reynolds	11-14-'46
Black, David	12-14-'44	Smith, Edward B.	11-14-'46
Book, M. Harold	12-14-'44	Conant, Robert F.	11-14-'46
Valdes-Dapena, Antonio	12-14-'44	Baumann, Elizabeth	11-14-'46
Boyle, Paul E.	1-11-'45	Butcher, James	11-14-'46
Buchanan, Edwin G.	3-8-'45	Breedis, Charles	12-12-'46
Farrar, George	4-12-'45	Rawson, A. J.	12-12-'46
Weidman, Charles	4-12-'45	Imbriglia, Joseph E.	1-9-'47
		Zeidman, Irving	1-9-'47

Reinstatements

Aronson, Roland L. (1946)
Brown, Clarke E. (1946)
Jennings, W. B. (1947)
Lieber, Marshall M. (1946)
Menkin, Valy (1946)
Norris, Robert F. (1946)

Resignations

Angevine, D. Murry (1946)
Aronson, Roland S. (1947)
Barthmaier, O. F. (1944)
Biggs, M. H. (1943)
Bratby, Forrest G.
Brown, H. I. (1942)
Cantarow, A. (1946)
Churchill, H. R. (1944)
Clark, J. Alexander (1944)
Egsville, John (1941)
Friedman, Melvin (1946)
Gruskin, Benjamin (1942)
Hawley, Sidney J. (1946)
Heinkele, Ethel R. (1946)
Jacobs, Maurice S. (1946)
Jacobsen, Sheldon A. (1942)
Kennedy, Patrick J. (1945)
Lund, Herbert (1942)
Meeker, George W. (1942)
McDonald, Ellice (1945)
Paul, John (1942)
Rose, Edward (1944)
Rose, S. Brandt (1947)
Soloff, Louis A. (1943)
Sutter, C. Clyde (1945)

Deaths

Abbott, W. O. (1943)
Brubaker, A. P. (1943)
Burr, Charles W. (1944)
Cattell, Henry W. (1936)
Fisher, Henry M. (1939)
Griffith, J. C. P. (1942)
Hughes, W. E. (1944)
McFarland, Joseph (1945)
Newlin, A. (1941)
Regester, Robert P. (1946)
Rosenberger, R. C. (1944)
Thornton, E. Q. (1945)

SPECIAL LECTURES

The Gross Lecture

1943. Lt. Col. Balduin Lucké: The Renal Lesions of the Crush Syndrome, Burns, and other Conditions Affecting the Lower Segments of the Nephrons.

The Conversational Lecture

1943. Shields Warren: The Effects of Radiation on Normal and Neoplastic Tissue.
1944. Col. George R. Callender: Diarrheal Diseases.

Catalogue of the Mütter Museum of the College of Physicians of Philadelphia

Part I

FOR almost one hundred years the Mütter Museum of the College of Physicians has existed with no published catalogue of its thousands of specimens.

When Dr. Thomas Dent Mütter's museum was presented to the College, in 1863, a printed catalogue accompanied it, but since the College already had a pathological museum, the two collections had to be united, and all specimens renumbered and reclassified, thus making Doctor Mütter's catalogue of little or no value.

Except for listing and numbering new specimens as they were received, little was done in the way of cataloguing until 1884, when Dr. Guy Hinsdale, the curator, undertook the enormous task of compiling the first complete and comprehensive catalogue. This consists of three large typewritten volumes. Through the years these suffered through much handling in making corrections and insertions, so in 1940 it was copied, giving the museum three new volumes which are also typewritten. In this first catalogue lengthy detailed descriptions are given in most instances, yet it is not a practical catalogue for use by the public, in locating desired material.

In 1946 Dr. Leandro M. Tocantins, a member of the Committee on the Mütter Museum, and Mr. W. B. McDaniel, 2d., the librarian and editor, conceived the idea of obtaining a simple published catalogue with a minimum of expense by having installments of it printed periodically in the *Transactions & Studies* of the College, and then assembling the reprints.

Before attempting this, various sources were consulted as to the best way to go about it, but strange to say, other museums of similar scope had no published catalogue either, and we were left more or less to our own devices.

A general plan has been mapped out that will be followed as closely as possible, although in a museum of over 7300 specimens one is bound to find some objects that defy classification. To avoid a lengthy and unsatisfactory "Miscellanous Section," as many of such objects as possible are listed in the classification into which they most nearly seem to fit.

The various specimens have been regrouped in many cases to make a more workable catalogue, and while detailed descriptions have been omitted for lack of space, anyone should be able to locate easily the type of specimen desired, and having located it, may then refer to the card file or consult the original catalogue for additional information.

Symbols are used in some instances to avoid tiresome repetition and also to conserve space. These are identified in the fore part of the catalogue.

The list of Donors and the Index will comprise the final installment.

A debt of gratitude is due Dr. Leandro M. Tocantins for his constructive criticism and kindness in taking time to review and correct each installment previous to publication, and to the two other members of the Committee on Mütter Museum, Dr. Oscar V. Batson and Dr. Paul C. Colonna, for their helpful suggestions.

The finished product will, it is hoped, prove to be of value and worth the time and effort that has been put into it.

Ella N. Wade
Curator

General Plan of the Mütter Museum Catalogue

PART I

Normal Anatomy

A. BONES
- 1. Skeletons
- 2. Skulls
- 3. Skulls—Hyrtle Collection
- 4. Bones of the Skull and Sections Showing Formations and Variations in Formations of the Head, Face and Sinuses.
- 5. Bones of the Spinal Column
- 6. Bones of the Thorax
- 7. Bones of the Upper Extremity
- 8. Bones of the Lower Extremity

B. ARTICULATIONS

C. SYSTEMS OF THE BODY
- 1. Blood-Vascular System
- 2. Lymphatic System
- 3. Nervous System
- 4. Digestive System
- 5. Respiratory System
- 6. Urogenital System

D. PRODUCTS OF CONCEPTION

E. SPECIAL SENSE-ORGANS
- 1. Eye
- 2. Ear

F. MUSCLES

G. SKIN

Key to the Mütter Museum Catalogue

A = Presented.
B = Purchased.
M = Model.
Cr. = Corrosional preparation.
CCC. = Possession of the College deposited in the Museum.
C (with number) = Illustration number in "Internal Anatomy of the Face," by Matthew Henry Cryer, M.D., 2d ed., Phila., Lea, [c. 1916].
Donors are indicated by numbers. The list of Donors and the Index will comprise the final installment.

PART I

Normal Anatomy

A. Bones

A. 1. Skeletons

Fetal

—from the second month of gestation to that of the child postpartum, articulated by the natural ligaments. 1000.40 A to 1000.40 J. B 5.
—from the third month to the end of gestation, disarticulated. 1001.25 A to 1001.25 F. B 5.
—third month. 1090.59. A 3.
—seventh month. 1000.60; 1000.75; 1000.50. A 1; A 2.
—eighth month. 1000.65. A 1.
—ninth month. 1000.45. A 1.

Adult

—female, age 24 years. 1145.40. B 5.
—male, age 30 years. 1145.20. B 5.
—male, age 32 years. 1145.25. B 5.
—of undetermined age and sex. 1002.00; 1145.10; 1002.05; 1002.10; 1002.15; 1002.20. A 1.
—articulated with its ligaments. 1004.00. A 1.
—incomplete. 17830.49.
—dried, from the collection of Prof. George McClellan. 17834.72. A 1.

A. 2. Skulls

(*See also:* A. 3. Hyrtl Collection.)

Fetal

—sixth or seventh month. 1006.88; 1008.85; 1098.01. A 14.
—eighth month. 1098.02.
—at term. 1098.03, 17836.05. A 59.

Child

—1006.84; 1006.85; 1006.86; 1006.87; 1008.835; 1008.845; 1006.846; 1008.41; with part of the outer table removed. 17831.12. A 14.
—head of an infant. (M) 17835.76; (M) 17835.77. A 11.

Adult

—with no special characteristics. 1006.249; 17830.49; 1007.00; 1007.01; 1007.02; 1007.03; 1007.04; 1007.05; 1007.07; 1008.09; 1007.10, 1007.11; 1007.12; 1007.13; 1008.03; 1008.04; 1008.51; 1008.57; 1008.62; 1008.67; 1008.72; 1008.73; 1008.765; 1008.775; 1008.78; 1008.785; 1008.81; 1008.815; 1008.825; 1008.826; head (M) 13505.00. A 1; A 12; A 14.
—(M) Chinese head after beheading. 8308.00. A 36.
—variously prepared
  —calvarium with outside cortical tissue removed. 1007.06; showing deep Pacchionian depressions. 1008.30. A 1.
  —disarticulated and mounted. 1008.00; 1008.10. B.
  —perforated to estimate the average thickness of the various portions of the cranium. 1007.15.
  —portion of the outer table removed showing diplöe, vascular and nervous distribution. 1008.05. B.
  —right half showing vascular supply of teeth. 1098.15.
  —left half showing nervous distribution. 1098.16.
  —cut to show sinuses and deeper anatomy. 1008.15; 1008.805. A 14.
  —vertical sections. 1007.14-A; 1007.14-B; 1008.21; 1008.22. A 1; A 12; showing internal membranes. 1008.25; 1008.26. A 12.
  —incomplete. 17835.80; 1008.02; 1008.28; 1008.53; 1008.745; 1008.75; 1008.795; 1006.72; 1006.73; 1006.75; 1006.78; 1006.79; 1006.80; 1006.81; 1006.82; 1006.83; 1023.21. A 1; A 11; A 12; A 14.
—identified
  —Chinese, from California. 1006.140. A 6.
  —Peruvian. 1006.142. A 7.
  —Sandwich Islands. 1006.143. A 7.
  —Caucasian. 1006.144; 1006.145. A 7.
  —Negro, female, age 20 years. 1006.146. B.
  —Irish, male. 1006.147. B.
  —Rebel killed in the first battle of Bull Run. 1006.77. A 10.
  —Catacomb of Rome (portion). 1167.40. A 9.
  —cannibal from Easter Island. 1008.35. A 13.

—Indian
—Sioux. 1006.248; Crow, from the Crow Agency in Montana. 1006.15; forty-eight from the Burial Mounds of Illinois near St. Louis and Geneva Lake, Wisconsin. 1006.200 to 1006.247. A 1; A 8.
—Neanderthal (M) 1006.50; (M) 1006.51. B 33.
—interior of the brain cavity. 1006.52 (M). B 33.
—Pithecanthropus Erectus (Trinial Man) (M). CCC. 1006.53. A 34.
—Eanthropus (Piltdown Man) (M). CCC. 1006.54. A 34.
—Sinanthropus Pekinensis. (M). CCC. 1006.55. A 34.
—variations
—extremely thin cranial bones. 1008.55. A 14.
—large and heavy. 1008.60. A 14.

A. 3. Skulls—Hyrtl Collection*

(*See also:* A. 2. Skulls.)

Austria

—Lower Austria. Male, age 13 years. (Armenia). 1006.061. B 4.
—Upper Austria. Male, age 19 years. (Armenia). 1006.062. B 4.
—a Jew. Male, age 41 years. 1006.003. B 4.
—Lissa Island. Male, age 39 years. 1006.133. B 4.
—Salzburg. Male, age 30 years. 1006.066; male, age 37 years. 1006.065; female, age 18 years. 1006.136. B 4.
—Styria. Male, age 48 years. 1006.138. B 4.
—Tyrol. Male, age 24 years. 1006.121; female, age 22 years. (Armenia). 1006.067. B 4.
—Vienna. Male, age 16 years. (Armenia). 1006.060; male age 16 years. (Armenia). 1006.063; male, age 29 years. 1006.002; female, age 19 years. (Armenia). 1006.059. B 4.

* Prof. Hyrtl's geographic locations have been left undisturbed, but place names have been Anglicized wherever this was feasible.

Hungary

—Hajdú. Male, age 21 years. 1006.015. B4.
—Cumania. Male, age 35 years. (Armenia.) 1006.071. B 4.
—a Magyar. Male, age 40 years. 1006.069. B 4.
—male, age 21 years. (Armenia). 1006.072. B 4.

Austria-Hungary

— a Magyar. Male. 1006.011; male, age 28 years. 1006.013. B 4.
—Ragusa. Male, age 28 years. 1006.132. B 4.
—Slavonia. Male, age 34 years. 1006.016. B 4.
—female, age 20 years. 1006.135. B 4.

Germany

—Silesia. Male, age 40 years. (Armenia). 1006.068. B 4.

Poland

—Galacia. Male, age 26 years. 1006.022; 1006.139; male, age 30 years. 1006.025; male, age 42 years. 1006.024; male, age 46 years. (Armenia). 1006.081; male, age 51 years. 1006.023; female, age 17 years. 1006.021. B 4.
—a Gorale. Male, age 43 years. (Armenia). 1006.083. B 4.
—Cracow. Male, age 26 years. (Armenia). 1006.082. B 4.

Switzerland

—a Cretin. Male. 1006.006; 1006.007; 1006.008. B 4.

Holland

—Amsterdam. Male. 1006.009. B 4.

Czechoslovakia

—Arva. Male, age 15 years. (Armenia). 1006.074. B 4.
—Bohemia. Male. (Austria). 1006.004; male, age 19 years. (Austria). 1006.001; male, age 25 years. 1006.131. B 4.
—Hanak. Male, age 25 years. (Armenia). 1006.084. B 4.
—male, age 25 years. (Armenia). 1006.079. B 4.

—Moravia. Male. (Austria). 1006.005. B 4.
—Ruthenia. Male, age 21 years. 1006.103. B 4.
—Slovakia. Male, age 39 years. (Armenia). 1006.073. B 4.
—Tablunka. Male, age 22 years. 1006.106. B 4.
—Zips. Male, age 34 years. 1006.014. B 4.

Yugoslavia

—Belgrade. Male, age 24 years. 1006.137; a Serb, male, age 30 years. (Turkey). 1006.026. B 4.
—Bosnia. Male. 1006.091. B 4.
—Carniola. Male, age 19 years. (Armenia). 1006.087. B 4.
—Croatia. Male, age 24 years, of mixed race, German and Croat. (Hungary). 1006.017. B 4.
—Dalmatia. Female, age 19 years. (Armenia). 1006.088. B 4.
—Montenegro. Male. (Turkey). 1006.029. B 4.
—Serbia. Male, age 24 years. 1006.090. B 4.
—Turkey. 1006.127. B 4.
—Zagreb. Female, age 21 years. 1006.126. B 4.

Romania

—Babadag. Male, age 13 years. 1006.093. B 4.
—Bukowina. Male, age 18 years. 1006.078; Gipsy, male, age 24 years. 1006.018. B 4.
—a Gipsy. Male, age 24 years. 1006.130. B 4.
—Giurgevo. Male, age 23 years. 1006.027. B 4.
—Maramuresh. 1006.012. B 4.
—Moldavia. A gipsy, male, age 31 years. 1006.031; Gipsy, male, age 37 years. 1006.098. B 4.
—male, age 25 years. 1006.096. B 4.
—Transylvania. Male, age 32 years. 1006.095; male, age 36 years. 1006.075; male, age 50 years. 1006.077. B 4.

Bulgaria

—1006.094.

Russia

—Alatyr. Male. 1006.105. B 4.
—Daghestan. 1006.125. B 4.
—Finland. Male. 1006.032. B 4.
—Caukasus. 1006.124. B 4.
—Cossacks. Male. 1006.101. B 4.
—Kostroma. Male. 1006.104. B 4.
—male, age 30 years. 1006.036; male, age 52 years. 1006.100. B 4.
—Scopzi. Male. 1006.035. B 4.
—Siberia. Male, age 35 years. 1006.033. B 4.

Armenia

—male, age 29 years. 1006.099; female, age 8 years. 1006.058; female, age 48 years. 1006.086. B 4.

Turkey

—a Kurd, male. 1006.028. B 4.

Syria

—a Maronite, male. (Turkey). 1006.030; male. 1006.122. B 4.

Persia

—Kashan, male, age 20 years. 1006.102. B 4.

Italy

—Albenga, Sardinia. Male. 1006.045. B 4.
—Aosta. Male. 1006.044. B 4.
—Aquileia. Male, age 50 years. 1006.041. B 4.
—Bergamo. Male, age 32 years. 1006.043. B 4.
—Calabria. Male. 1006.048. B 4.
—Elba. Male, age 24 years. 1006.114. B 4.
—Friuli. Male, age 30 years. 1006.118. B 4.
—Genoa. Male, age 15–17 years. 1006.113. B 4.
—Lombardy. Male, age 21 years. 1006.119. B 4.
—Naples. Male, age 13 years. 1006.112. B 4.
—Parma. Male, age 14 years. 1006.108. B 4.
—Ragusa, Sicily. Male, age 37 years. 1006.047. B 4.
—Ravenna. Female, age 20 years. 1006.116. B 4.
—Rome. Male, age 28 years. 1006.046; from the Catacombs. 1006.129. B 4.
—Trieste. Male, age 20 years. 1006.120. B 4.

—Tudicaria. Female, age 18 years. 1006.109. B 4.
—male, age 15 years. 1006.115. B 4.
—Quarnero Islands. Female, age 23 years. 1006.042. B 4.

Greece

—Albania. 1006.097; male. 1006.123. B 4.
—Brazza Island. 1006.051; male, age 29 years. (Armenia). 1006.089. B 4.
—Candia, Crete. Male. 1006.054. B 4.
—Cephalonia. Male. 1006.053. B 4.
—Corfu. Male. 1006.057. B 4.
—Hydra Island. Male. 1006.056. B 4.
—Morea. Male. 1006.055. B 4.

Siam

—male. 1006.039. B 4.

Egypt

—from king's tomb. 1006.040; mummy from Thebes. 1006.128. B 4.

China

—Hong-Kong. Male. 1006.049. B 4.

Japan

—Tokyo. 1006.050. B 4.

A. 4. Bones of the Skull and Sections Showing Formations and Variations in Formations of the Head, Face and Sinuses

Calvarium

—1023.00; 1023.05; 1023.10; 1023.15; 1023.20. A 1; A 12.

Frontal bone

—1011.00; 1011.05; 1011.10; 1011.15. A 1.

Mandible

—from birth to eighteen months. 1023.306, C-1. A 14.
—of a child. 1021.50; 1021.55. A 1.
—age about seven months, with central incisors erupted. 1098.04.
—ten months, with eight incisor teeth erupted. 1098.05.
—one and one-half years with sixteen teeth erupted and permanent teeth visible imbedded in upper jaw. 1098.06.
—two years, with eruption of sixteen teeth. 1098.07.
—three years, with eruption of twenty temporary teeth. 1098.08.
—seven years. The lower middle incisors and first molar permanent teeth of the upper and lower jaws have assumed their proper position. 1098.09.
—eight years. The central and lateral lower incisors and first molar teeth of the lower jaw and the central incisor teeth and first molar teeth of the upper jaw are in situ. 1098.10; 1098.11.
—eleven years. Both canine of the upper jaw have erupted. 1098.12.
—twelve years. The canine and first molar teeth have only partially descended. 1098.13.
—showing obliquity of the ramus. 1098.17.
—showing the approximation to a right angle in the relation of the ramus to the body of the bone. 1098.18.
—of adult. 1021.60 through to 1021.71; 1021.75; 1023.22; 1023.23; 1023.437; 1023.437 A, C-109-119; 1023.307; 1098.14. A 1; A 12; A 14.
—of old age. 1021.00; 1021.05; 1021.10; 1021.15; 1021.20; 1021.25; 1021.30; 1021.35; 1021.40; 1021.45; 1023.422; 1098.20; 1023.308, C-4. A 7; A 12; A 15; A 14.
—showing obliquity of the ramus. 1098.19.
—horizontal section
—cut in the region of points of the roots of the teeth. 1023.384, C-44; 1023.441, C-43. A 14.
—made at necks of 16 mandibular teeth. 1023.310, C-115. A 14.
—made at necks of 14 mandibular teeth. 1023.311, C-114. A 14.
—showing forms and positions of the roots of the various teeth. 1023.441, C-43. A 14.
—lateral section
—showing relation between the condyloid process of mandible and mandibular fossa, the external meatus and the parotid gland. 1023.410, C-63. A 14.
—longitudinal division
—exposing cancellous tissue in body of the

jaw and between sockets of the teeth. 1023.394; 1023.394 A, C-40. A 14.
—vertical section. 1021.81; 1021.82; 1021.83. A 12.
—with external cortical portion of bone removed. 1021.80; 1023.407, C-35; 1098.25, C-31-32; 1008.49, C-31-32. A 14; A 1.
—with teeth removed. 1023.3041, C-34. A 14.
—showing
—cribriform tube (mandibular canal). 1023.349, C-33. A 14.
—four premolars on each side. 1023.309, A (M). A 14.
—showing
—open spaces in the body of, (M) 1023.392; 1023.393, C-41-42. A 14.
—variations in distance between the two condyles and from the condyle to the incisor teeth. 1023.304. A 14.
—portion of. 1021.86; 1021.87; 1021.871; 1021.872; 1021.873; 1023.443. A 12; A 14.
—showing roots of the third molar passing through the inner wall into the submaxillary fossa. 1023.430, A-60. A 14.

Maxilla

—1015.00; 1015.05; 1015.10; 1015.15; 1015.20; 1015.25; 1015.30; 1015.35; 1098.14. A 1.
—with external cortical portion of bone covering the roots of the teeth removed. 1008.49, C-31-32. A 14.
—of a child, age about
—seven months. 1098.04; ten months. 1098.05; one and one-half years. 1098.06; two years. 1098.07; three years. 1098.08; seven years. 1098.09; eight years. 1098.10; 1098.11; eleven years. 1098.12; twelve years. 1098.13. (See mandibles having same numbers for information on teeth).
—showing six premolar teeth, (M). 1023.309, C-342. A 14.

Occipital bone

—1009.00; 1009.10; 1009.15; 1009.20; 1009.25; 1009.05. A 1; A 12.

Parietal bone

—1010.00; 1010.05; 1010.15; 1010.20; 1010.25; 1010.30; 1010.10; 1010.35; 1010.40; 17830.50; 17830.51. A 1.

Sphenoid bone

—1013. A 1.
—portion of. 1013.05; 1013.10. A 1.

Temporal bone

—1012.00; 1012.05; 1012.10; 1012.15; 1012.20. A 1; original specimens showing a simple mastoid operation. 1012.50; 1012.51; showing a radical mastoid operation. 1012.52. (Article on "Determination of the Line of the Descending Portion of the Facial Canal in Doing the Mastoid Operation," by Frank Bridgett, M.D., The laryngoscope, May 1923, Vol. 33, p. 329). A 60.
—mastoid cell of. (Cr.) 10008.00. B 4.
—portion of. 1012.17. A 1.

Sinuses

—antrum
—accessory cells in wall between antrum and nasal chamber. 1023.334. A 14.
—bony septum in both. 1023.317. A 14.
—communicating with the anterior ethmoid cells. 1023.346; 1023.348. A 14.
—extending into the zygoma. 1023.316. A 14.
—invasion of, by the roots of the molar teeth. 1023.314; 1023.363. A 14.
—large, with irregular architecture favoring the retention of secretions during irrigation. 1023.323. A 14.
—openings into, very high, making drainage impossible. 1023.330. A 14.
—two openings from, to the nasal chamber. 1023.315; 1023.318; 1023.325; 1023.333. A 14.
—unusually large opening into. 1023.327. A 14.
—unusually thin anterior wall. 1023.332. A 14.
—frontal
—drainage into the left infundibulum. 1023.388. A 14.
—extending into the cribriform plate. 1023.363; under the orbit. 1023.337, C-105; extending from within the great wing of the sphenoid bone forward to the frontal bone, then backward to the sphenoid bone. 1023.426, C-254-255-256. A 14.
—five; anterior view and four complete septa. 1023.375, C-246. A 14.

—four. 1023.358, C-101-245. A 14.
—large. 1023.362; 1023.367, 1023.376, C-249, 1023.396; 1023.396 A, C-253; 1023.426; right. 1023.436, C-250-296. A 14.
—extending under the orbit. 1023.364. A 14.
—with thick anterior wall. 1023.381. A 14.
—showing incomplete septa. 1023.374, C-252.
—small, in an extremely thick frontal bone. 1023.379, 1023.436. A 14.
—three, with three individual outlets and two complete septa. 1023.378, C-244-295. A 14.
—with thin anterior wall. 1023.370. A 14.
—1023.365. A 14.

—maxillary
—bony septum in. 1023.331; 1023.336; 1023.339. A 14.
—cuboidal in shape. 1023.358, C-101-245. A 14.
—division through. 1023.401, C-215-216. A 14.
—globular in shape. 1023.329. A 14.
—large. 1023.328; 1023.343, C-216; 1023.353, C-103, 1023.358; 1023.367, C-260, 1023.378, C-244-295; 1023.401, C-215-216; 1023.411, C-174-216. A 14.
—membranous septum in upper anterior angle of. 1023.324. A 14.
—passing into the zygoma. 1023.382, 1023.382 A, C-271. A 14.
—peculiar shape. 1023.440, C-212. A 14.
—posterior views of two vertical sections made from different skulls in about the same anatomical region, showing great variations as to depth of face and size and shape of nasal cavities and maxillary sinuses. 1023.373, C-284-261. A 14.
—sections showing floor of nasal cavity, alveolar process and floor of maxillary sinus are nearly on the same level. 1023.436, C-250-296. A 14.
—small. 1023.319; 1023.337, C-105; 1023.344, C-194.
—with thick floor. 1023.326; 1023.397; 1023.439; 1023.439 A. A 14.
—variations. 1023.391; 1023.397; 1023.397 A, C-213-214; 1023.398, C-109. A 14.
—with crescent-shaped cells. 1023.403, C-207. A 14.
—with two openings. 1023.320. A 14.
—with many accessory pockets. 1023.321; 1023.335. A 14.
—roof of. 1023.377, C-279. A 14.
—1023.372; 1023.361, C-231, 1023.402. A 14.

—orbital
—large supra-orbital sinus. 1023.367, C-260. A 14.

—sphenoidal
—1023.365. A 14.
—large. 1023.343, C-216; 1023.350; 1023.351; 1023.351 A; 1023.401, C-215-216; 1023.411, C-174-216; 1023.438, C-258; 1023.367, C-260. A 14.
—ostia of, at different levels. 1023.345. A 14.
—with accessory cells. 1023.347. A 14.

Section in the region of the orbit

—anteroposterior division through the center of the orbit, maxillary sinus and molar teeth, showing
—peculiar shaped sinus. 1023.440, C-212. A 14.
—enlarged cell of the orbital process of the palate bone. 1023.397; 1023.397 A, C-213-214. A 14.
—triangular cell at the upper posterior corner of the maxillary sinus. 1023.398, C-209. A 14.
—crescent-shaped cell at upper posterior corner of maxillary sinus. 1023.403, C-207. A 14.
—horizontal section through orbits and ethmoid cells and sphenoidal sinuses. 1023.438, C-258. A 14.
—large supra-orbital sinus. 1023.367, C-260. A 14.
—infra-orbital sinus. 1023.361, C-230. A 14.

Ethmoid Cells

—antra communicating directly with the ethmoid cells. 1023.346, 1023.348. A 14.
—horizontal section through. 1023.438, C-258. A 14.
—large. 1023.345. A 14.
—1023.365. A 14.

A. 5. Bones of the Spinal Column

Atlas

—1024.05; 1024.06. A 1; A 12.
—and axis. 1024.07.

Cervical vertebrae

—1024.00; 1024.10; 1024.11; 1024.15; 1024.20; 1024.25; 1024.30. A 1; A 12.
—spinous process. 1025.15. A 12.

Dorsal and thoracic vertebrae

—1025.25; 1025.30, 1025.35; 1025.40; 1025.45; 1025.50; 1025.55; 1025.56; 1025.57; 1025.58; 1025.60. A 1; A 12.
—vertical section. 1025.61; 1025.62; 1025.63; 1025.64. A 12.
—with lumbar vertebrae and radius. 1037.27. A 12.
—spinous process. 1025.15. A 12.

Lumbar vertebrae

—1026.00; 1026.05; 1026.10; 1026.15; 1026.23; 1026.25; 1026.26; 1026.29. A 1; A 12.
—vertical section. 1026.20. A 1.
—spinous process. 1025.15. A 12.
—with dorsal vertebrae and radius. 1037.27. A 12.

Sacrum

—vertical section. 1027.00; 1027.05 A; 1027.05 B; A 1; A 17.
—and ilium. 1045.00. A 17.
—and innominate. 1045.75; 1045.80; 1045.85. A 1.

Vertebral column

—1025.05; 1025.10; 1025.12. A 1.
—with pelvis. 1025.00. A 1.
—and right innominate and upper portion of femur. 1047.00. A 12.

Vertebrae

—948-Misc. CCC. A 8.
—portion of. 1025.20. A 12.
—and pelvis. 17834.49; 17834.50; 17834.53. A 11.
—showing non-union of the epiphyses in a man age 23 years. 1185.00. A 18.
—horizontal section. 1025.65. A 17.
—vertical section. 1026.31. A 17.

A. 6. Bones of the Thorax

Thorax

—1031.00; 1031.05. A 1; A 18.

Ribs

—thirty-one; 1031.01 through to 1030.31. A 1; A 12.
—portion of. 1031.32. A 12.
—vertical section. 1030.33. A 1.

Sternum

—1029.00; 1029.05; 1029.10; 1029.15; 1029.20· A 1; A 12.

A. 7. Bones of the Upper Extremity

Clavicle

—1032.20; 1032.25; 1032.30; 1032.35; 1032.36; 1032.37; 1032.38, 1032.39; 1032.40; 1032.41; 1032.42. A 1; A 12.
—horizontal section. 1032.15 A; 1032.15 B. A 1.
—longitudinal sections. 1032.00; 1032.05; 1032.10. A 17.
—vertical section. 1032.16. A 12.
—and scapula. 1033.30; 1033.31; 1033.315. A 12.
—and humerus. 1035.15. A 12.
—and upper portion of the humerus showing the joint. 1035.10. A 12.

Scapula

—1033.00; 1033.05; 1033.10; 1033.15; 1033.20; 1033.21; 1033.22; 1033.23; 1033.24; 1033.25. A 1. A 12.
—portion of. 1033.26. A 12.

Arm

—(M) 8707.10. A 37.
—and hand, articulated. 1040.15; 1040.20. A 12.

Humerus

—1034.35; 1034.40; 1034.45; 1034.50; 1034.55; 1034.60; 1034.65; 1034.70; 948-Misc. CCC· A 1; A 12. A 8.
—vertical section. 1034.30 A; 1034.30 B. A 1.
—of superior half. 1034.00; 1034.05; 1034.10; 1034.15. A 17.
—of condyles. 1034.20. A 17.
—of head. 1034.25 A; 1034.25 B. A 1.
—with radius and ulna. 1036.05.

—vertical section, of a child. 1039.00. A 17.
—with scapula and clavicle. 1035.15. A 12.
—upper portion showing joint, with scapula and clavicle. 1035.10. A 12.
showing non-union of the epiphyses, from a man age 23 years. 1005.05 C. A 18.

Radius

—1037.15; 1037.20; 1037.23; 1037.24; 1037.25; 1037.26. A 1; A 12.
—vertical section. 1037.10 A; 1037.10 B. A 1.
—of extremity. 1037.00; 1037.05. A 17.
—of carpal end. 1037.22; 1039.10; 1040.10. A 12.
—transverse section of carpal end. 1037.21. A 12.
—with dorsal and lumbar vertebrae. 1037.27. A 12.
—with humerus and ulna. 1036.05.
—vertical section. 1039.00. A 17.
—and ulna. 1039.01; 1039.02; 1039.051; 1039.08; 1039.10; 1039.11; 1039.12; 1039.13; 1039.14. A 12.
—transverse section. 1039.04; 1039.06; 1039.09. A 12.
—of carpal end. 1039.05. A 12.
—of ulna. 1039.03. A 12.
—of radius. 1039.07. A 12.
—and carpals, metacarpals and first phalanges. 1040.05. A 12.
—and hand. 1040.10. A 12.

Ulna

—1038.05; 1038.10. A 1.
—vertical section of extremities. 1038.00. A 17.
—and radius. 1039.01; 1039.02; 1039.051; 1039.08; 1039.10; 1039.11; 1039.12; 1039.13; 1039.14. A 12.
—transverse section. 1039.04; 1039.06; 1039.09. A 12.
—of radius. 1039.07. A 12.
—of carpal ends. 1039.05. A 12.
—of ulna. 1039.03. A 12.
—vertical section of carpal end of radius. 1039.10. A 12.
—with carpals, metacarpals and first phalanges. 1040.05. A 12.
—and humerus. 1036.05.

Bones of the hand

—articulated. 1040.05; 1044.00; 1044.25; 1044.26; 1040.00. A 1; A 7; A 12; A 17.
—disarticulated. 1044.50. A 1.

A. 8. Bones of the Lower Extremity

Pelvis

—infant. 17834.51. A 11.
—child. 17834.55 (M). A 11.
—adult. 1045;50; (M) 1365.31; (M) 17835.78; (M) 17835.79; 17834.47, (M) 17834.52. A 1; A 11.
—and upper part of femur. 17834.46. A 11.
—and vertebral column. 1025.00. A 1.
—and vertebrae. 17834.49; 17834.50; 17834.53. A 11.

Innominate bone

—1045.38; 1045.39; 1045.41; 1045.42; 1045.43; 1045.44; 1045.45; 1045.46; 1045.47; 1045.48; 1045.49. A 1; A 12.
—portion of. 1045.35; 1045.36; 1045.40 A; 1045.40 B; 1045.40 C. A 1; A 12.
—and sacrum. 1045.75; 1045.80; 1045.85. A 1.

Ilium

—1045.40; 1045.405.
—and head of femur; vertical section. 1045.20; 1045.30. A 17.
—and portion of vertebral column and upper portion of femur. 1047.00. A 12.
—and sacrum, vertical section. 1045.00. A 17.

Femur

—1046.35; 1046.40 through to 1046.50; 1046.62; 1046.63, 1046.65. A 1; A 12.
—vertical section. 1046.29 A; 1046.29 B; 1046.30 A; 1046.30 B; 1046.52; 1046.53; 1046.54. A 1; A 12.
—of head. 1046.02, 1046.05, 1046.10, 1046.11. A 17; A 19.
—of lower end. 1046.15, 1046.20. A 17.
—of condyle. 1046.51; 1046.55; 1046.56. A 12.
—transverse section. 1046.55; 1046.58; 1046.61. A 12.
—of condyle. 1046.57; 1046.59. A 12.

—upper portion. 1046.51; 1046.60; 1046.66; 1046.70; 1047.00. A 12.
—and part of pelvis. 17834.46. A 11.
—lower portion. 1046.67; 1046.68; 1046.69, 1047.71, 1048.05. A 12.
—showing non-union of the epiphyses, from a man age 23 years. 1005.05 B. A 18.
—and tibia of a child, vertical section. 1046.25. A 17.
—and tibia and fibula. 1005.16; 1005.17.
—and skull of Pithecanthropus Erectus. (M) CCC. 1006.53. A 34.

Left leg. 1047.03.

Cast of leg. (M) 8191.65.

Tibia

—1049.45; 1049.50, 1049.55; 1049.65; 1049.70; 1049.75. A 1; A 12.
—and femur of a child; vertical section. 1046.25. A 17.
—vertical section. 1049.38; 1049.39; 1049.40 A; 1049.40 B; 1049.40 C. A 1.
—of head. 1049.00; 1049.05; 1049.10; 1049.15; 1049.16 A; 1049.16 B. A 1; A 17.
—of lower end. 1049.20; 1049.25; 1049.30; 1049.35. A 17.
—vertical and transverse section. 1049.41; 1049.42. A 12.
—and fibula. 1051.00. A 1.
—and femur. 1005.16; 1005.17.
—and astragalus. 1051.15.
—and right foot. 1052.00; 1051.04. A 12.
—showing non-union of the epiphyses, from a man age 23 years. 1005.05 A. A 18.

Fibula

—1050.05; 1050.10; 1050.15. A 1.
—vertical section. 1050.00 A; 1050.00 B. A 1.
—and tibia. 1051.00. A 1.
—and femur. 1005.16; 1005.17.
—and astragalus. 1051.15.
—and right foot. 1052.00; 1051.04. A 12.
—femur, tibia and patella. 1048.05. A 12.

Patella

—1057.05; 1057.10; 1057.15; 1057.20; 1057.25; 1057.35. A 1; A 12; A 20.
—transverse section. 1057.30. A 12.
—with knee-joint, femur and fibula. 1048.05. A 12.

Calcaneum and astragalus

—1053.05.
—vertical section. 1053.00. A 17.

Bones of the foot, articulated and disarticulated

—1056.00; 1056.25; 1056.50; 1056.55. A 1; A 7; A 12; A 17.
—ligamentous preparation. 1060.00. A 21.
—tibia and fibula. 1052.00; 1051.04. A 12.

B. Articulations

Shoulder-joint

—showing ligaments. 1035.00. A 17.
—vertical section. 1035.05. A 17.
—with scapula, clavicle and humerus. 1035.10 A 12.

Elbow-joint. 1036.00. A 12.

Wrist-joint and hand. 1040.00. A 17.

Knee-joint

—1048.00. A 1.
—and part of femur, fibula and patella. 1048.05. A 12.

C. Systems of the Body

C. 1. Blood-Vascular System

Heart

—fetal, with lungs. 1077.10.
—of child. 1066.00.
—of adult. (M) 8130. B.
—laid open. (M) 8814. B.
—with pericardium. (M) 8812; (M) 8813.

Arteries

—in axillary region. (M) 8004. B 42.
—bronchial artery (ramifications) Cr. 10052.00. B 4.
—bronchial and pulmonary artery of right inferior lobe of a human lung. Cr. 10049.00. B 4.
—of left lung. Cr. 10050.00. B 4.
—in body of a child at term. (Dried preparation) 1090.55; 1090.57.
—in seventh month embryo. Cr. 10002.00. B 4.
—in foot. 10045.00. Cr. B 4.
—in hand. 1068.05, 1068.10; (M) 8110.00; Cr. 10044.00. A 1; B 4.
—head and thorax; superficial arterial distribution. (M) 8002.00. B 42.

—in intestinal tract. (M) 8008.00.
—in liver
—of child. Cr. 10035.00. B 4.
—of adult. Cr. 10037.00. B 4.
—in lumbar vertebral column of a child. Cr. 10046.00. B 4.
—maxillary and its branches. (M) 8001.5.
—in skull. 1068.00; 1008.05. A 1; B.
—in tongue. 10042.00. Cr. B 4.

Veins

—in body of a child at term (dried preparation). 1090.55; 1090.57.
—portal vein system of a child of 10 months. Cr. 10036.00. B 4.
—in hand. 1068.10; (M) 8110.00.
—in head and thorax. (M) 8002.00. B 42.
—in inguinal region. (M) 8005. B.
—portal and hepatic vein in liver of a child. Cr. 10035.00. B 4.
—portal vein in human liver. Cr. 10037.00. B 4.
—in lumbar vertebral column of a child. Cr. 10046.00. B 4.
—in skull. 1008.05. B.
—in posterior thoracic and abdominal cavities. (M) 8006.00. B.
—in teeth. 1098.15.

C. 2. Lymphatic System

Lymphatics of the

—axillary region, (right thorax and arm). (M) 8004. B.
—bladder. 2219.00 B 41.
—canal of Fontana. 2216.00. B 41.
—clavicular region and neck. (M) 8003.00. B.
—ear. 2212.00. B 41.
—and nasal cavities. 2214.00. B 41.
—foot. 2218; 2224. B 41; B 42.
—genitals, external, female. 2223.00. B 42.
—hand. 2217.00. B 41.
—inguinal region. (M) 8005. B.
—lips. 2213.00. B 41.
—nasal cavities
—and ear. 2214.00. B 41.
—origin of. 2215.00 B 41.
—neck and clavicular region, head and thorax. (M) 8003.00. B.
—penis, scrotum and groin. 2222.00. B 42.
—scalp. 2204.00. B 41.
—and portion of neck. 2001.00; 2002.00. B 41.
—face and ear. 2203.00. B 41.
—origin of. 2205.00. B 41.
—thoracic and abdominal cavities. (M) 8006.00. B.
—thoracic duct and vertebral column. 2221.05. B 42.
—tongue, fauces and epiglottis. 2211.00. B 41.
—dorsum of, the fauces and epiglottis and artenoepiglottidean fold from a woman age 35 years. 2206.00; from a child. 2207.00. B 41.
—and larynx; lower side. 2208.00. B 41.
—and hard palate. 2209.00. B 41.
—vertebral column of man. 2219.05. B 42.

C. 3. Nervous System

Brain

—(M) 1083.00; (M) 8252. A 8; B.
—base of. (M) 8250.00. B.
—cerebellum with medulla, spinal cord plexuses and nerves. (M) 8025.00. B.
—microscopic sections prepared by Dr. Henry D. Schmidt. 1083.01 to 1083.37.
—of man, magnified. (M) 8021; normal size. (M) 8022.00. B.
—sections. (M) 17830.70; (M) 8435.00.
—with spinal cord and nerves. (M) 8020.00.
—tracts of brain stems. 17830.71.
—showing ventricles, choroid and plexus. (M) 8270.00.
—head sections. 13300.00; 13300.01; 13300.02; 13300.03; 13300.05; 13300.07; 13300.08; 13300.09; 13300.10. A 38.
—lantern slides. 17832.87. A 43.

Nerves of

—axillary region. (M) 8004.00. B.
—hands. 1068.05; 1068.10. A 1.
—head and thorax. (M) 8002.00; head. (M) 8001. B.
—intestinal tract. (M) 8008. B.
—skull. 1008.05; 1068.00.
—brain and spinal cord. (M) 8020. B.
—cerebellum, medulla and spinal cord. 8025.00. B.

Spinal Cord

—with brain and nerves. (M) 8020.00. B.

—with cerebellum, medulla, plexus and nerves. (M) 8025. B.
—dissection exposing cauda equina. 1084.00.

C. 4. Digestive System

Tongue

—and surrounding parts. (M) 8125.
—arteries of. 10042. Cr. B 4.

Teeth and their development

—in fetal skull
  —of six months; the septa marking the sockets are faintly seen. 1098.01.
  —of eight months; sockets are better marked. Upper incisors are descended but visible. 1098.02.
  —at term. Alveoli, and showing the temporary teeth undescended. 1098.03.
  —in right half of skull showing all the permanent teeth and their vascular supply. 1098.15.
  —in left half of skull showing nervous distribution. 1098.16.
—jaw bone
  —of a child of seven months. The central incisor teeth have erupted. 1098.04.
    —ten months. Eight teeth have erupted. 1098.05.
    —one and one-half years. Eruption of sixteen teeth. 1098.06.
    —two years. Eruption of sixteen teeth. 1098.07.
    —about three years. Eruption of twenty temporary teeth. 1098.08.
    —about seven years. 1098.09.
    —eight years, showing teeth in proper position. 1098.10; 1098.11.
    —about eleven years. Both canine teeth of the upper jaw have erupted. 1098.12.
    —about twelve years. The canine and first molar teeth have only partially descended. 1098.13.
  —showing all the permanent teeth except the wisdom teeth have assumed their position. 1098.14.
  —anterior lateral view of upper and lower, with external cortical portion of the bone covering the roots of the teeth removed. 1008.49. C-31-32. A 14.
  —temporary teeth. 1098.23.
    —and permanent teeth of upper jaw. 1098.21.
    —previous to eruption. 1098.22.
  —permanent teeth. 1098.24.

Teeth and variations

—alveolar process. 1023.360, C-60; deep. 1023.439; 1023.439 A; showing floor of nasal cavity, alveolar process and floor of maxillary sinus nearly on the same level. 1023.436, C-250-296. A 14.
—molar teeth
  —invading the antrum. 1023.314; 1023.363. A 14.
  —three pieces of bone with molar teeth that have been accidentally broken away with part of the floor of the maxillary sinus in an extraction. 1023.362, C-231-232-233. A 14.
  —section cut in the region of the molar teeth. 1023.366, C-281-268-292-292. A 14.
—cancellous tissue between the sockets of the teeth. 1023.394; 1023.394 A. A 14.
—premolar teeth
  —vertical section of negro skull between the second premolar and first molar. 1023.368. A 14.
  —ground section of six anterior teeth and two left premolars. 1023.416, C-36. A 14.
  —maxilla showing six premolar teeth. (M) 1023.309. C-342. A 14.
—roots
  —section showing conical elevations over roots of various teeth; the root of the second premolar curves forward while it more commonly curves backward. 1023.390, C-202-203; 1023.417. A 14.
  —of third molar passing through the inner wall into the submaxillary fossa. 1023.430, C-60. A 14.
  —horizontal section of maxilla and mandible showing forms and position of the roots of various teeth. 1023.441, C-43. A 14.
—variations
  —anteroposterior division through the center of the orbits, maxillary sinus and teeth showing variations. 1023.397;

1023.397 A, C-213-214; 1023.398, C-209; 1023.403, C-207. A 14.

Abdomen

—posterior thoracic and abdominal cavities, showing the receptaculum chyli in the median line. (M) 8007. B.

—section of abdomen and thorax. (M) 17830.36. A 35.

Intestinal tract, showing ileocaecal valve. (M) 8008. B.

Liver

—fetal. 1090.00.

—of a child, with artery and portal veins. 10035.00, Cr. B 4.

—adult, with artery, portal veins and cystic ducts. 10037.00, Cr. B 4.

Duct of Wirsung. 10034.00, Cr. B 4.

C. 5. Respiratory System

Bronchus; ramification and bronchial artery. 10052.00, Cr. B 4.

Larynx. 1078.00, 1078.10; A 15; A 22.

Lungs and heart of a fetus. 1077.10.

Throat and respiratory passages. (M) 8120.00. B.

Thoracic viscera of a fetus. 1077.00. A 15.

Variations in formations in the region of the nose

—two openings from the antrum to the nasal chamber. 1023.315; 1023.318; 1023.336. A 14.

—one opening leading from the antrum to the nasal chamber. 1023.333. A 14.

—accessory cell between the antrum and nasal chamber. 1023.334. A 14.

—inferior turbinate extends above the opening into the antrum. 1023.322; under the surface of inferior concha and the outlet to the nasolacrimal duct. 1023.408, C-179. A 14.

—horizontal section cut just above the floor of the nasal cavity, which is very wide. 1023.344, C-194. A 14.

—narrow arch and wide floor of nose. 1023.352; 1023.352 A, C-100; 1023.354, C-102; 1023.366. A 14.

—wide arch and narrow nose. 1023.355, C-99; 1023.358. A 14.

—maxillary sinus extends below the floor of the nasal cavity. 1023.358. A 14.

—vertical section through the nasolacrimal duct showing the infra-orbital canal and maxillary sinus. 1023.402, C-175. A 14.

—nasal cavity

—lateral wall of. 1023.411, C-174-216. A 14.

—with middle concha and portion of cell wall turned up. 1023.425, C-172-180-204. A 14.

—large. 1023.366, C-281-268-292-293. A 14.

—upper portion. 1023.377, C-279. A 14.

—section showing variations as to depth and size in the external wall and nasal cavities. 1023.359; 1023.359 A, C-285-286; 1023.373. A 14.

Sinuses—See: A. 4. Bones of Skull and Sections Showing Formations and Variations in Formations of the Head, Face and Sinuses.

C. 6. Urogenital System

Urinary Organs

Kidney

—infant. 4301.00. A 24.

—adult. 1093.00.

—laid open. (M) 8815.00.

—dorsal and ventral halves. 10009.00 Cr. B 4.

—different forms of the human pelvis of the kidney, namely, a negro; a pregnant woman; assymetry of left and right from a man age 40 years; with double ureter and pelvis; of a new born child. 10025, Cr. B 4.

Male Reproductive Organs

—pelvic organs. (M) 8040.00; (M) 8045. B.

—seminal vesicle unrolled. 10047.00, Cr. B 4.

Female Reproductive Organs

—generative organs. 1089.10; 17835.79; (M) 8050.00; (M) 8055; (M) embryology of man 1090.001. B; A 11; A 18.

—of an infant of eight days. 1089.35. A 24.

—showing position of uterus in relation to the cervix. 1089.01. A 23.

—Uterus and appendages. 1089.00. A 23.

—at one month, (M) 1090.002; second month. (M) 1090.003; third month.

(M) 1090.004; fourth month. (M) 1090.005; eighth month. (M) 1090.006; ninth month. (M) 1090.007.

—with fetus in situ. 1089.65; 1089.70.

D. Products of Conception

Embryo

—1090.05; 1090.051; 1090.07; 1090.085; 1090.10. A 18.

—and chorion. 1090.08. A 18.

—and membranes. 1090.09; 1090.11. A 18; A 27.

—second month. 1090.12; 1090.18; twins. 1090.50. A 18; A 32.

—with uterus. 1090.046.

—third month. 1090.045; 1090.049; 1090.16; 1090.17; 1090.20; 1090.21; 1090.22. A 15, A 18; A 23.

—with membranes. 1090.13; 1090.15. A 18.

Fetus

—1090.211; 1090.405. A 20; A 29.

—prepared by the Schultze method. 1090.044. A 25.

—fourth month. 1090.047; 1090.19; 1090.23; 1090.24.

—with membranes. 1090.14. A 18; A 24. A 28.

—with placenta. 1090.27. A 18.

—fifth month. 1090.25; 1090.32; 1090.37; 1090.375; 1090.40. A 18.

—with placenta. 1090.28; 1090.29; 1090.30; 1090.31; 1090.33; 1090.34; 1090.35. A 18.

—and membranes. 1090.26. A 27.

—sixth month. 1090.38; 1090.425; 1090.43; 1090.46; 1090.405. A 18; A 30.

—in membrane. 1090.048. A 20.

—with placenta. 1090.365; 1090.42. A 20; A 7.

—and placenta. 1090.41. A 18.

—and cord. 1090.56.

—eighth month.

—in utero. 1090.45.

—ninth month. 1090.44. A 31.

Membranes of fetus and embryo

—1090.052, 1090.053; 1090.048; 1090.049; 1090.09; 1090.42; 1090.11, 1090.13, 1090.14, 1090.15, 1090.26, 1090.365, 1090.42. A 20; A 27; A 18.

Ovum showing chorial villi. 17836.04. A 59.

Blighted ovum. 1090.06. A 26.

Placenta

—10055.00, Cr., 10056.00 Cr., 10057.00, Cr., 1090.7509, Cr. through to 1090.7524, Cr.; 1090.26, 1090.27, 1090.28; 1090.29; 1090.30; 1090.31; 1090.33; 1090.34; 1090.35; 1090.365; 1090.41; 1090.42; 1090.56. B 4; A 18; A 20; A 27.

—cotyledonous. 1090.60. A 27.

—of twins. 1090.7503 through to 1090.7508, Cr. B 4.

—of triplets. 1090.7501, Cr.; 1090.7502, Cr. B 4.

E. The Special Sense-Organs

Eye

—(M) 8105.00. B.

—spirals of the lacrimal duct and the spiral valve of the lacrimal sac. (Eight preparations). 10001, Cr. B 4.

—For normal and pathological anatomy of the eye see also: Part VIII. Lantern slides. 17832.85. A 81.

Ear

—(M) 8115.00. B.

—mastoid cell of temporal bone. 10008.00, Cr. B 4.

—temporal bone showing simple mastoid operation. 1012.50; 1012.51; showing a radical mastoid operation. 1012.52. A 60.

—tympanic membranes, series by Adamus Politzer. 1100.201 to 1100.267. A 45.

—normal. 1100.201 to 1100.226; 1100.245; 1100.247, 1100.248 to 1100.258; 1100.263 to 1100.266.

—pathological. 1100.227 to 1100.244; 1100.246; 1100.259 to 1100.262; 1100.267.

—lymphatics. 2203.00; 2212; 2214.00. B 41.

—ossicles of

—embryo. 1059.001; 1059.002; 1059.003. B 4.

—new born infant, with temporal bone, exterior. 1059.004, interior 1059.005. B 4.

—youth. 1059.006. B 4.

—Hottentot. 1059.008. B 4.

—old man. 1059.007. B 4.

—Egyptian mummy. 1059.009. B 4.

—cyclops. 1059.011. B 4.
—anencephalic monster. 1059.012. B 4.
—bicorporate monster. 1059.13. B 4.
—labyrinths of
—embryo of five months. 1100.00; six months. 1100.001; eight months. 1100.003; seven months. 1100.002; at maturity. 1100.004. B 4.
—infant at age of two years. 1100.005. B 4.
—youth of twenty years. 1100.006. B 4.
—Hottentot youth. 1100.008. B 4.
—man of ninety years. 1100.007. B 4.
—female deaf mute. 1100.009. B 4.
—man, in situ. 1100.010. B 4.
—For normal and pathological anatomy of the ear see also: Part VIII. Lantern slides. 17832.84; 17832.85. A 81, A 82.

F. Muscle

Face and neck

—(M) 8100.00. B.
—the side, with skin, fasciae and some of the muscles removed. (M) 8112.00. B.

G. Skin

Vertical section showing hair follicles and sweat glands. (M) 8150.00. A 12.

TRANSACTIONS & STUDIES

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The Treatment of Infective Asthma with Penicillin in Beeswax and Oil*

By LESLIE N. GAY, M.D., AND HENRY J. L. MARRIOTT, M.D.
With the Technical Assistance of Louis L'Archeveque

WHEN the medical profession reviews the estimates of chronic disease in the United States, its members will immediately be impressed by the high incidence of respiratory disability. In 1936, the United States Public Health Service (1) published the following figures of chronic disease:

Rheumatism and Arthritis	6,850,000
Heart Disease	3,700,000
Hay Fever and Asthma	3,450,000
Chronic (asthmatic) Bronchitis	1,700,000

There were thus 5,150,000 individuals who either had asthmatic symptoms or were potential asthmatic patients. In World War I, 2.45 per thousand young men were rejected by draft boards because of this disease; fifteen years later, among every 1000 veterans who received disability compensation, 12 were compensated because they had developed asthma during their military service. In regard to the discharged soldiers of World War II, there is as yet no figure available to tell us of the future disability or of the compensation required.

Of these five million, many have become allergic to some extrinsic factor or factors, but by and large the majority have developed or will develop asthmatic bronchitis secondary to invasion by some bacterial agent. It is needless to detail the development of the latter disease, but we wish to emphasize that the terms bacterial asthma, infectious asthma and intrinsic asthma are synonymous. The symptoms with which you are familiar are recurrent, are worse in bad weather, and they invariably occur after over-exposure. These symptoms are disabling in the same manner as are those symptoms which develop in an individual who is specifically sensitive to some extrinsic material such as pollen, animal dander or some food.

Time will not permit a detailed discussion of the differential diagnosis of Bronchial Asthma due to bacterial allergy and Bronchial Asthma due to infection, the latter commonly called Asthmatic Bronchitis. Even

* Lecture delivered before the Section on General Medicine of the College of Physicians of Philadelphia, April 28, 1947.

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The Penicillin Levels were determined in the Biological Laboratory of the Johns Hopkins Hospital. The penicillin in wax and oil was contributed by E. R. Squibb & Sons. The authors express their appreciation.

among the most experienced, bacterial allergy as related to asthma is not clearly understood. Unlike the tuberculin test in tuberculosis, bacterial skin tests in asthma reveal no information of value. However, there are a number of good reasons for the assumption that infection (that is, bacteria themselves or their products) is a cause of an allergic response which may manifest itself as asthma. The most convincing evidence of the allergic nature of infectious asthma is the fact that a reaction may frequently be elicited by means of small doses of vaccine, especially one made from an autogenous vaccine.

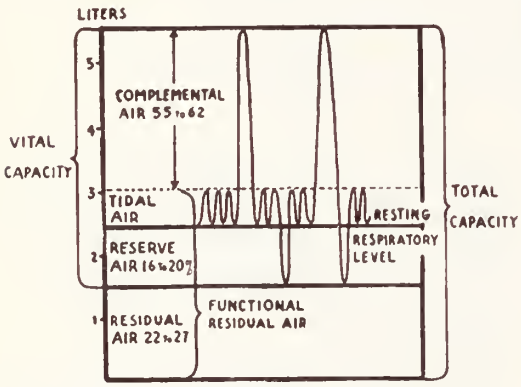

FIG. 1. SUBDIVISIONS OF LUNG AIR
(From Best and Taylor)

Furthermore, we believe that infection of the bronchi and the respiratory tract can by itself without allergy cause the disease known as asthma. For this disease "asthmatic bronchitis" may be the preferred term, but irrespective of the name, the symptoms in the two manifestations are the same.

This report includes both types, for it has been impossible to determine with certainty whether bacterial allergy is responsible or whether infection without allergy accounts for the symptoms in the group of patients that have been treated with Penicillin in Wax and Oil.

The physiology of respiration must be understood in order that the rationale of the treatment of asthma can be comprehended. The structure of the chest permits enlargement by the forward-and-upward movement of the anterior chest. The angle of the ribs and their attachments allow lateral expansion, while the diaphragm enlarges the chest in forward and downward directions. Thus under normal conditions, all lobes expand in inspiration and all bronchi elongate and dilate.

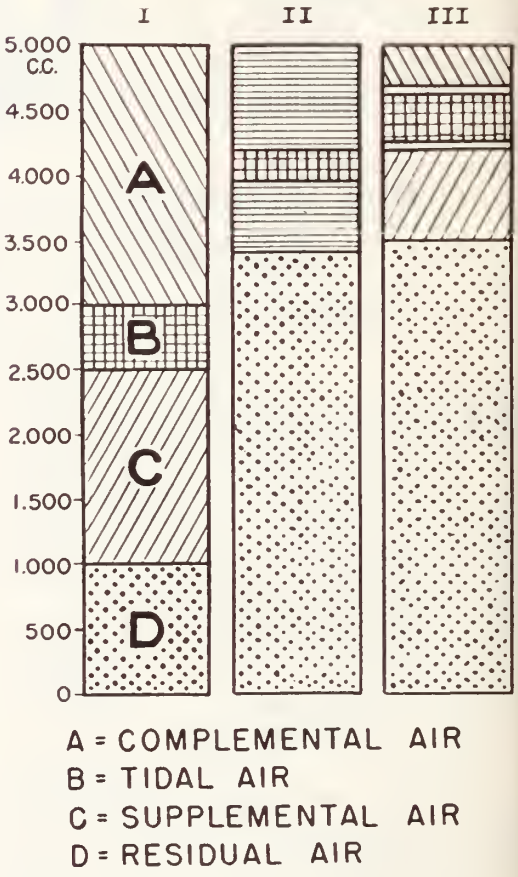

FIG. 2. DIAGRAM SHOWING SUBDIVISIONS OF THE LUNG AIR IN ASTHMA (II) AND EMPHYSEMA (III) COMPARED WITH THE NORMAL (I)
(From Best and Taylor)

Conversely, in expiration the lobes relax and the bronchial tree constricts and shortens. In quiet respiration the intrapleural pressure is a negative pressure (Fig. 1, 2):

Quiet Inspiration....	−3 to −6 mm. Hg.
Quiet Expiration....	−1 to −3 mm. Hg.
Forceful Inspiration with Obstruction..	−40 mm. Hg.
Forceful Expiration..	+50 mm. Hg.

Consider the asthmatic patient whose chief difficulty is experienced in expiration. Because the pressures are greatly altered, the partition of air in the lungs becomes abnormal. Residual air is greatly increased; complemental air and supplemental air are diminished to zero. The chest is in a state of full expansion and the patient is exerting the greatest inspiratory and expiratory efforts of which he is capable. Most important is the great reduction in the vital capacity of the asthmatic patient both during an attack and between the paroxysms, when the patient is comparatively comfortable. Even when the patient pursues his daily routine without complaint, an abnormal respiratory pattern is present, as demonstrated in the physiology laboratory of the New York Presbyterian Hospital (2):

(1) Marked impairment of the bellows action of the chest persists even after the asthmatic patient is free from symptoms. This is demonstrated by a decrease of maximum breathing capacity from the predicted value for the individual subject (58% of normal).

(2) Hyperventilation is noted during rest, during a minute of standard exercise, and during the first minute of recovery.

(3) Alveolar nitrogen following oxygen breathing is abnormally high; the mean value for the group is 4.5%.

In acute asthma a state of extreme ventilatory insufficiency develops. Hyperventilation persists in order to keep narrowed bronchial passages dilated sufficiently to permit ventilatory air exchange. All accessory muscles of respiration are brought into the effort. Acute emphysema, which rapidly develops, soon lowers vital capacity from a normal figure to as low as 600 cc. of air. If the acute attacks recur frequently, then a chronic state develops as a result of oedema of bronchial walls and exudation of mucus and cells into the lumen of the bronchi and alveoli. These mucous plugs often completely obstruct the lumen of bronchi and bronchioli so that smaller or larger areas of lung tissue become atelectatic or areas of collapse develop adjacent to areas of emphysema.

The clinical diagnosis of obstructed bronchi is not difficult, for these patients show suppressed breathing in one or both lower lobes. Although the patient is in respiratory distress, rales are greatly diminished in one or both of the lobes. Lipiodol, used only for diagnosis, will confirm or disprove the clinical impression. The dislodgement of the plugs, by whatever means, will give symptomatic relief. These abnormalities were demonstrated in the autopsy material of the Johns Hopkins Hospital. Practically all of the 24 asthmatic patients autopsied revealed plugged bronchi (3).

The treatment of bronchial asthma with penicillin is not new. The literature is replete with references.

During the past two years bronchial asthma of infectious or 'intrinsic' type has been attacked with penicillin in various forms and by various routes: subcutaneous or intramuscular injections of aqueous solutions, oral preparations and a variety of inhalational methods have been used. Results of treatment by these methods have been reported on as follows:

A. BY INJECTION

Sweeney *et alii* (4) report seven cases treated with one to five million units over an average period of 14 days; there was initial but unsustained improvement.

Leopold and Cooke (5) report two cases successfully treated with 100,000 units daily for 10 and 14 days respectively. Both patients remained free from symptoms for four months.

Kaufman (6) reports one case treated with two-hourly doses of 10,000 units up to a total of 1,900,000 units; the patient remained asymptomatic for two months.

Leopold (7) reports 86 cases of asthma treated with 40,000 units every four hours for 7 to 45 days. The cases are divided into two groups (a) 62 with chronic infectious asthma of whom 26 derived symptomatic

improvement, but only 10 of these remained free from symptoms for any length of time; and (b) 23 with chronic allergic asthma with superimposed acute bronchitis of whom only 4 were improved.

Miller (8) reports on 29 cases who received an average of 1,300,000 units in three-hourly doses. In a follow up of 4 to 18 months, 14 out of the 29 derived varying degrees of lasting benefit.

B. BY INHALATION

Barach (9) reported moderate improvement in 8 out of 12 cases treated by aerosol for 5 to 12 days.

Vermilye (10) claims to have obtained "very successful" results in 25 cases.

Segal and Ryder (11) report 6 cases whose clinical course was unaltered by aerosol penicillin, although sensitive organisms were eliminated from bronchial cultures.

Hagens *et alii* (12) report 4 cases of whom two were improved and two unimproved.

Kay and Meade (13) report 19 cases of chronic bronchitis treated by intratracheal instillation; an unspecified number had asthma and were said to be considerably improved.

Hurst (14) treated 4 cases by nebulizer of whom two showed marked improvement.

Engelsher (15) reports 74 cases of whom only 15% (11) were slightly improved by aerosol administration.

Fullerton (16) reports 4 cases with no improvement from aerosol therapy.

Finke (17) reports on 10 patients with "mixed allergic-infectious" asthma; the response was variable, and best results were obtained by combining aerosol with control of extrinsic factors.

Pyle (18) reports 3 cases of bronchial asthma complicated by bronchiectasis and treated with aerosol. Penicillin sensitive organisms disappeared from their sputa, but no comment is made on the effect on asthmatic symptoms; the somewhat naive remark is made that the underlying pathology was unchanged.

Humphrey *et alii* (19) report 20 cases of "chronic bronchitis with spasm": All were improved and the authors comment "asthma improved pari passu with the bronchitis, often to a striking extent".

Southwell (20) reports 17 cases of "chronic bronchitic asthma", of which 1 was cured, 13 improved, and 3 showed no improvement.

Toch *et alii* (21) report 1 case which responded well.

C. ORAL

Baumann *et alii* (22) report 36 patients so treated with 60,000 units three-hourly for 3 days. 26, or 71%, were temporarily controlled.

György (23) reports a good result in a three year old child who received 25,000 units every four hours.

D. COMBINED METHODS

Schonwald and Deppe (24) treated 86 cases of asthma with combined subcutaneous and oral penicillin. They summarize their cases in a way that does not assist in a statistical review of the results of penicillin therapy in intrinsic asthma; of the 86 cases 69 were asthmatic: of the total of 86 cases 21 were intrinsic allergies and 65 "mixed"; of the 86, 34 were markedly improved, 35 moderately improved and 16 not improved at all. No indication is given of the proportion of the 21 cases of intrinsic asthma which improved.

Hampton *et alii* (25) report 7 cases who received from 500,000 to 1,300,000 units intramuscularly. This was followed at a later date by intratracheal treatment with pressure spray. Two further cases were treated by spray alone. Slight clinical improvement is reported in 4 of the 9 cases. Vital capacity studies in this group are recorded and showed a general tendency to increase with treatment.

Toch *et alii* (21) report 3 cases which responded to inhalation plus intramuscular therapy.

To give a general impression of the proportion of successes claimed for each method of treatment Tables A, B, C, D have been compiled from those reports in which exact figures were given by the authors. Numerical

exactitude obviously gives a false impression of accuracy unattainable in a study of this sort, and so it is emphasized that the data collected is intended only as the roughest of indications. The Tables show a total of 337 cases treated by all methods reported on with an overall improvement realized in 143 or 42½%.

TABLE A

INTRAMUSCULAR

AUTHOR	TOTAL CASES	IMPROVED	NOT IMPROVED
Sweeney	7	0	7
Leopold and Cooke	2	2	0
Kaufman	1	1	0
Leopold	62 23	10 4	52 19
Miller	29	14	15
Totals	124	31	93

I.e., improvement in 25%.

TABLE B

INHALATIONAL

AUTHOR	TOTAL CASES	IMPROVED	NOT IMPROVED
Barach	12	8	4
Vermilye	25	25	0
Segal and Ryder	6	0	6
Hagens *et al.*	4	2	2
Hurst	4	2	2
Engelsher	74	11	63
Fullerton	4	0	4
Humphrey	20	20	0
Southwell	17	14	3
Totals	166	82	84

I.e., improvement in 50%.

No reports have been published on the treatment of intrinsic asthma with large doses of penicillin in oil and beeswax. This method of adminstration has obvious advantages over all others, particularly in that the patient can remain ambulatory with the inconvenience of only one injection a day and yet attain adequate concentrations of penicillin throughout the twenty-four hours. He thus avoids hospitalization or frequent visits to office or clinic with consequent loss of time which other methods of administration entail. The following cases shown in Tables A to D are therefore submitted.

I. The Selection and Preliminary Studies of the Cases

This report comprises twenty-two patients seen in private practice and seventeen patients seen in the out-patient clinic of the Johns Hopkins Hospital. Each patient had suffered with asthma which had been brought on by infection in the respiratory tract, and in no case had any extrinsic factor influenced the precipitation of the patient's symptoms. The symptoms had always been more severe and the asthmatic attacks occurred more frequently during the months from October to May, although in many of the cases attacks occurred throughout the entire year.

TABLE C

ORAL

AUTHOR	TOTAL CASES	IMPROVED	NOT IMPROVED
Baumann	36	26	10
György	1	1	0
Totals	37	27	10

I.e., improvement in 73%.

TABLE D

COMBINED

AUTHOR	TOTAL CASES	IMPROVED	NOT IMPROVED
Hampton	7	0	7
Toch	3	3	0
Totals	10	3	7

I.e., improvement in 30%.

After each patient had been selected for treatment, the following studies were carried out:

1. The sedimentation rate was determined.

2. The reaction of each patient to bacterial antigens injected intracutaneously prior to treatment was compared with the reaction to similar injections after the completion of the treatment.

3. The sputum was cultured, the organisms were differentiated and their sensitivity to penicillin was determined.

4. For documentary evidence penicillin blood levels were determined in every patient six hours after the third injection, six hours after the seventh injection and twenty hours after the tenth injection.

5. Vital capacity was calculated in each patient before the first treatment, during the course of treatment and at the completion of the treatment.

Of all these studies, the last physiologic test was the best indication of the success or failure of the therapeutic method.

II. Material and Method of Treatment

The material used in this therapeutic trial was contributed by E. R. Squibb & Sons. Ten cc. vials of amorphous penicillin calcium in wax and oil (each containing 300,000 units to the cc.) were used in preference to the single cartridge of 300,000 units to a cc., as the vial was more convenient to handle and more economical.

Each patient received *600,000* units in 2 cc. of wax and oil, the injection was made into the buttocks, each day for ten days. The administration of such a large dose requires a special technique. Variation from these instructions is probably the cause of the local reactions repeatedly mentioned in the review of the literature. Prior to injection, the ten cc. vial of penicillin in wax and oil (P.O.B.) is kept in a water bath of 60°C. for 15 minutes. When the rather solid material softens after heating, the bottle requires shaking. An intramuscular needle of 20 gauge is used to withdraw 2 cc. of the semifluid P.O.B. into a dry, slightly warmed 2 cc. syringe. The injection is immediately made into either buttock, and after the usual technique to ascertain that the needle has not entered a blood vessel, the contents of the syringe is slowly injected into the muscle. The syringe is then detached from the needle, one and one half cc. of air is drawn into the syringe, the syringe is reattached to the needle and the air is injected in order to clear the channel of the needle of P.O.B. If this last step is omitted from the procedure, a local reaction may occur because the P.O.B. will be sucked from the channel of the needle into the subcutaneous tissue at the time of withdrawal.

During ten days, 6,000,000 units of penicillin were thus injected. Penicillin levels were determined after the third dose, after the seventh dose and after the tenth dose. For several patients the time of determination varied somewhat, and the levels were determined in these exceptions after the fourth dose and after the eighth dose. Sedimentation rates were repeated in a number of cases. Throughout the first ten days of treatment the vital capacity was checked against the test run prior to treatment.

In order to maintain the initial improvement which resulted from the first ten doses, each patient receives a booster dose of 600,000 units every five to seven days. The booster dose will be continued until the danger of infection from varying weather conditions is at a minimum. More recently crystalline penicillin G sodium has been used in preference to the amorphous penicillin calcium because of certain advantages over the older product.

III. Results of Treatment

In the September issue of the Journal of Allergy 1946 (26), Louis Tuft discussed "Oral Penicillin in Treatment of Bacterial Asthma". Those of us who have had long experience in the treatment of this disease fully realize the ease with which therapeutic results are credited to new drugs, therefore, Tuft's discussion is quoted in part: "It is quite natural that the newer chemotherapeutic drugs should be tried in patients with a condition as stubborn and unresponsive as so-called 'infectious asthma'. The sulfonamides were the first to run the

gamut of enthusiasm and subsequent disappointment. As far as one could judge, they provided little benefit except perhaps in the prevention or treatment of infectious complications. Penicillin is the latest to join the ranks of panaceas for asthma, and while some favorable reports have appeared as to its use, our own limited experience with it has been disappointing, up to now.... No one can doubt ... that patients treated with penicillin are benefited somewhat, even though its duration is temporary. *However, one must seriously question in this or similar types of treatment whether the beneficial effect can be attributed to the effect of the agent itself or more likely to other measures instituted at the same time.*"

The last sentence (which we have italicized) is most important, and is equally true whether the therapy is directed toward the relief of asthma or any other chronic disease. We wish to emphasize that as far as possible all of the measures used in the treatment of chronic infectious asthma were discontinued; three patients, however, were so ill that they had to be hospitalized. These exceptions will be discussed in detail.

The clinical course of the majority of the twenty-two patients seen in private practice was remarkable in that relief followed the third or fourth injection of penicillin. The usual cough subsided; the wheezy dyspnoea decreased to normal breathing; the sputum became abundant and was raised with ease. Patients enjoyed a far greater freedom of chest movement, and during the course of injections physical signs in the chest gradually cleared; in areas where plugged bronchi had been found prior to treatment, breath sounds were now normal.

With the completion of the ten doses two observations were made: first, it was difficult for the patient to cough up sufficient sputum specimens for bacteriologic study; second, the sedimentation rate in the majority of cases had increased. The diminished amount of sputum paralleled the clinical relief, a result that was to be expected. The increased sedimentation must be further investigated. A possible explanation is that it is due to the reaction which occurs about the wax and oil as these materials are slowly absorbed by the tissue fluid.

Before the treatment was begun, the reaction of the patients to bacterial antigens, injected intracutaneously, had been considered of questionable value. Still the opportunity to study the possible effect of large doses of penicillin on such reactions was not lost. The majority of the patients reacted to one or more of the ten organisms which were administered as simple intracutaneous tests. There was no change whatever in the individual reactions that occurred prior to treatment and subsequent to treatment. This procedure therefore can be considered as superfluous.

Bacteriologic examination of the sputa before treatment demonstrated a mixed flora in all thirty-nine patients. Mixed strains of Streptococci predominated in 25 specimens, nonhemolytic Staphylococci were found in 16 specimens, Pneumococci grew from 15 specimens, nonpathogenic Neisseria were found in 12 specimens, and in 2 specimens Proteus was isolated.

The qualitative sensitivity of these organisms to penicillin was determined by the very simple procedure developed by Sir Alexander Fleming. A blood-agar plate streaked with sputum was divided by a straight line. A few drops of salt solution containing ten units of crystalline penicillin per cc. were cascaded over one half of the plate; the excess solution was pipetted off as it collected in the lower margin of the plate and discarded. The plate was incubated for 24 hours, then observed. With the exception of two sputa the areas washed over with penicillin revealed no colonies, but the control areas were over-run. In one of the two exceptions, the growth of the organisms was completely retarded by the substitution of 100 units of crystalline penicillin to the cc. In the second exception a Streptococcus grew profusely, even though a solution of 100,000 units of penicillin to a cc. was used. In spite of this, the patient received treatment and the clinical result was among the most successful (Fig. 3).

After the completion of the preliminary treatment (6,000,000 units of P.O.B.) striking changes were observed in the organisms isolated from the sputa. Whenever a specimen could be obtained, the number of colonies was greatly reduced over the control area. However quantitative evaluation of the bacterial flora of the sputum is difficult, as the results obtained depend upon the manner of streaking the plate and on the consistency of the sputum.

Furthermore, before treatment mixed strains of Streptococci grew from the sputa of twenty-five patients, after treatment these organisms were grown from the sputa of sixteen patients; a non-hemolytic Staphylococcus, grown from the sputa of sixteen patients before treatment, was found in only eleven sputa after treatment; the Pneumococcus isolated from the sputa of fifteen patients before treatment was recovered from five sputa after treatment. The Neisseria were apparently not affected by the treatment; in the two sputa from which Proteus grew before treatment, this organism could not be recovered after treatment (Table E).

TABLE E

Sputa Cultures

Organism	Bacteriologic studies	
	Before treatment	After treatment
Streptococci, mixed strains	25	16
Staph. albus, non-hemolytic	16	11
Pneumococci	15	5
Neisseria, non-pathogenic	12	14
Proteus	2	0

The penicillin blood levels, determined empirically 6 hours after the 3rd and 7th doses, and 20 hours after the 10th dose have contributed documentary evidence that the antibiotic was in the circulation. The figures have been so variable that no specific conclusions can be reached from the limited data that have been collected. It is the considered opinion of Dr. Harry Eagle that blood levels do not reveal the actual amount of penicillin in contact with the infected part, but they tell us whether the concentration of penicillin is sufficient for therapeutic activity (Fig. 4).

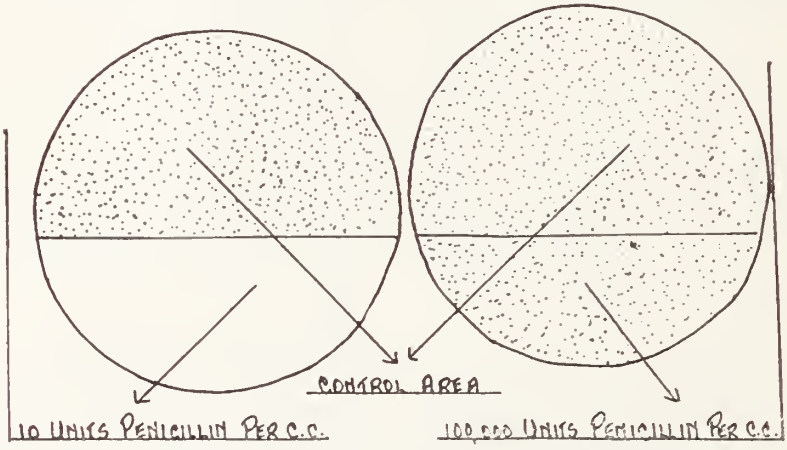

Fig. 3. Bacterial Sensitivity Plate after 24 Hours Incubation with Aqueous Pencillin

Left: non-hemolytic staph.; right: hemolytic staph.

Vital capacity, the physiological test, increased. This increase was gradual as was learned by repeated observations during the ten days of treatment. After the tenth dose, the vital capacity in all patients who derived any benefit from the treatment reached an approximation of the normal expected volume. Thirty-one of the thirty-nine patients showed an increase by this respiratory gauge. Compared with the capacity prior to treatment, this increase has been as much as 200 per cent. The absence of plugged bronchi, the reduction of dyspnoea and the gradual increase in com-

plemental and supplemental air in the lungs and bronchial tree contribute to the improvement in the vital capacity. The patients who derived no benefit continued to cough, respiration was as labored as before the treatment

doses of P.O.B. only four have had a recurrence of asthmatic symptoms. Several patients have developed mild upper respiratory infections, but in contrast with the usual course of events, severe attacks of prolonged

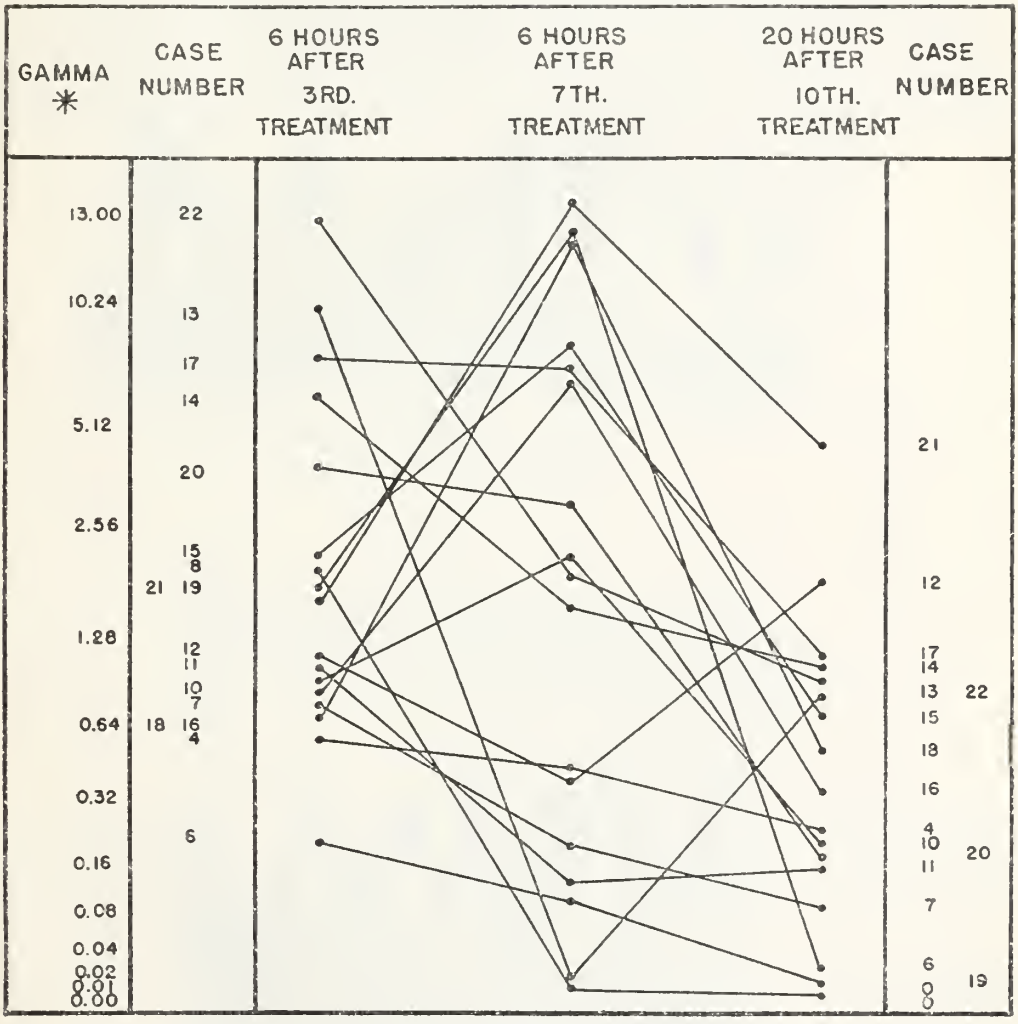

Fig. 4. Penicillin Blood Levels—1 Gamma = 1.66 Units

was commenced, and physical signs persisted in the chest (Figs. 5, 6).

The booster dose of 600,000 units has been given every five to seven days in order to control any infection which might occur, and the result obtained has justified the procedure.

In this group of 22 private patients, there are 3 failures. Of the 19 who received booster asthma, during these episodes the patients have been free from respiratory embarrassment.

The 17 patients treated in the dispensary of the Johns Hopkins Hospital are considered separately because less favorable results should be anticipated in a group of persons who must either walk to the hospital in bad weather or

wait for transportation. Often they return to inadequately heated, or over-heated, homes. are especially gratifying. These seventeen patients had been chronically ill and had been

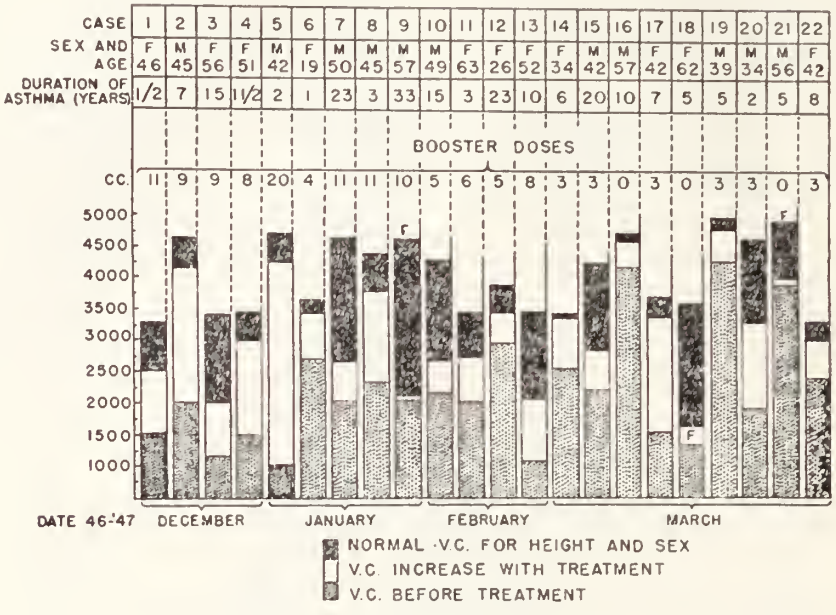

FIG. 5. F = FAILURE

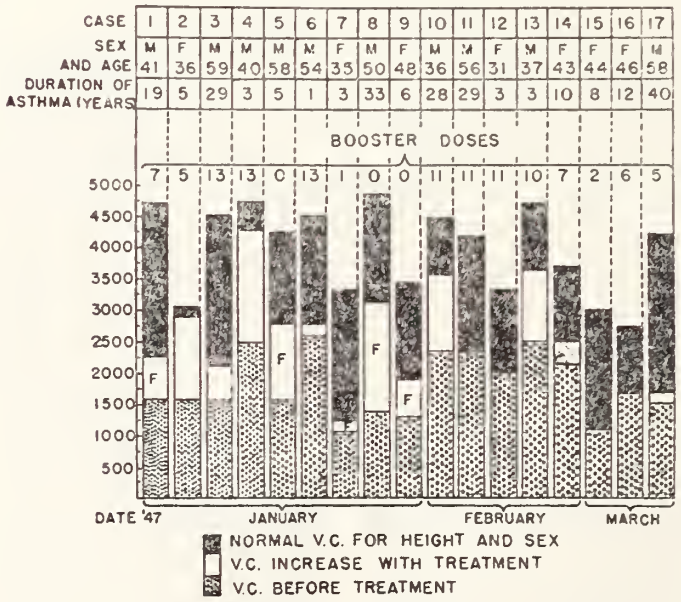
CASE 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17
SEX AND AGE M 41 F 36 M 59 M 40 M 58 M 54 F 33 M 50 F 48 M 36 M 56 F 31 M 37 F 43 F 44 F 46 M 58
DURATION OF ASTHMA (YEARS) 19 5 29 3 5 1 3 33 6 28 29 3 3 10 8 12 40
BOOSTER DOSES
7 5 13 13 0 13 1 0 0 11 11 11 10 7 2 6 5
5000
4500
4000
3500
3000
2500
2000
1500
1000
500
F
DATE '47 JANUARY FEBRUARY MARCH
NORMAL V.C. FOR HEIGHT AND SEX
V.C. INCREASE WITH TREATMENT
V.C. BEFORE TREATMENT

FIG. 6. F = FAILURE

For obvious reasons their circumstances did not contribute any aid to this form of treatment. In spite of these handicaps, our results frequent visitors in the dispensary on clinic days and many of them in the accident room both at night and during the day.

In the series of 17 cases, five are failures in whom no sustained improvement occurred. The remaining twelve have definitely improved while under treatment; three of these have obtained complete or almost complete relief from symptoms. Estimates of relief were based on reduction in frequency and severity of attacks, reduction in cough and sputum, decrease in requirements of symptomatic medication and increase in vital capacity.

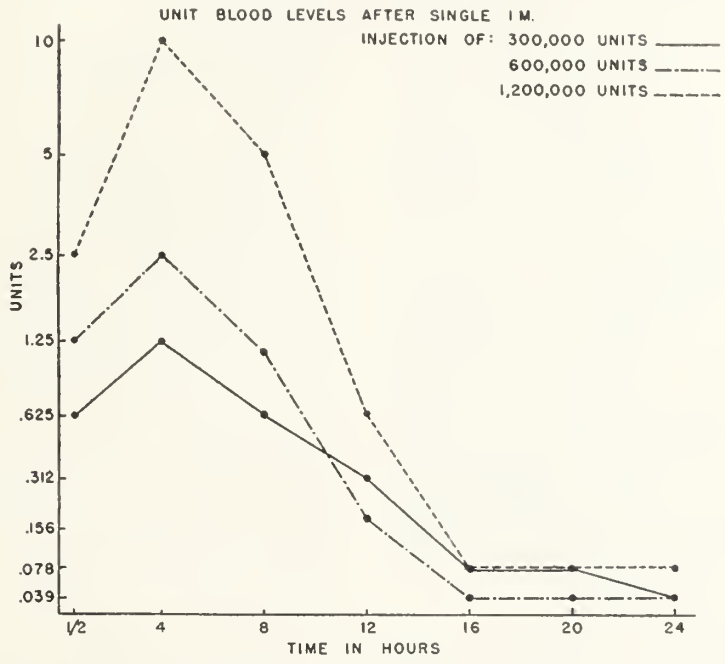

FIG. 7. A. Romansky: New England M. J., **233:** 577, 1945. Blood Levels After Intramuscular POB. *300,000* units POB in *1 cc* produce effective blood levels for *24 hours* and continued urinary excretion of penicillin for *3–4 days*. *Cumulative effect:* after daily injection for 8 days there is continued urinary excretion *for 6 days* following last injection. 600,000; 900,000; or 1,200,000 units does not much increase *time* of assayable levels in blood. 300,000 units at *12 hourly intervals* maintains level at or above 0.312, with peak of 1.25 units.

Nine patients have gradually reduced all medication to an occasional inhalation of adrenalin solution 1:100, and an occasional ephedrine capsule. As a group these seventeen patients have reacted less favorably than the private group. Still reference to the vital capacity chart reveals a most gratifying increase in their respiratory function.

DISCUSSION

In 1944 Romansky (27) reported a method of prolonging the action of penicillin by combining the antibiotic with beeswax and oil. In 1945 (28) he suggested that a single daily dose of 300,000 units in 4.8 per cent beeswax in oil contained in 1 cc. should be adequate for all but overwhelming infections. A single injection of 600,000 units does not double the time during which assayable levels are present in the blood. This amount does produce extremely high levels which are effective for twenty-four hours with excretion in the urine for thirty-two hours. When a single daily dose of 600,000 units in 2 cc. is given for eight days, penicillin continues to be excreted in the urine for approximately six days following the last injection. Therefore, the amount of antibiotic which was administered to these patients with chronic infectious asthma was more than sufficient to overcome the infection, and the booster doses after the preliminary 6,000,000 units should be adequate to control recurring infection (Fig. 7).

The efficacy of treatment in an individual

appears to be unpredictable inasmuch as results bear no relation to age of patient, duration of asthma, sputum flora, sedimentation rate, eosinophilia, or reaction to bacterial skin tests. For example, of the fifteen private patients who derived complete relief from asthma, nine had had chronic asthma for more than seven years, six had had the disease for fewer than five years. Three of the nine patients had been afflicted with asthmatic symptoms for more than twenty years. During the course of treatment, and in spite of booster doses, four patients who had had asthma for two years, three years, ten years and twenty-three years respectively, suffered minor relapses. But in each instance relief was quickly obtained by the administration of a dose of penicillin. The three patients who derived no relief were selected because prior to the advent of penicillin, all remedies had failed to give relief. They had developed irreversible pulmonary changes as a consequence of prolonged asthmatic distress. One patient, age 59, had had asthma for thirty-three years. The other two patients, age 65 and 56, had had asthma for five years. The sputa of these three patients contained penicillin sensitive bacteria; still there was no improvement in their subjective symptoms, though in two cases the vital capacity increased slightly.

The five failures among dispensary patients comprised a miscellaneous group: one, a male of 58, had had asthma for 5 years and showed marked emphysematous changes; though his vital capacity increased by 75% he had no subjective improvement. A second, a male of 50, had suffered from asthma for 33 years and had marked emphysema; his vital capacity more than doubled during treatment but his subjective status remained unaltered. The third, a male of 41 had had asthma for 19 years and was moderately emphysematous; initial improvement during therapy was not sustained despite a moderate increase in vital capacity. The fourth, a female of 48, had had asthma for 6 years and had shown a significant sensitivity to the inhalants, but her present perennial asthma was thought to be at least greatly aggravated by a superimposed infection; she however showed no response to penicillin. The fifth, a woman of 35, had a thirty-three year history of asthma, and a past history of pulmonary tuberculosis; her x-ray showed considerable residual fibrosis with no evidence, however, of active infection; she had showers of crepitant rales at both apices which cleared markedly with treatment; though her asthma improved during the course of therapy, this improvement was not sustained.

There are many reports of local and general reactions during and after treatment with penicillin. Local reactions can usually be avoided by the technique described. However, an Arthus phenomenon can follow intramuscular injection, as was the case in one of the patients in this report, and booster doses were discontinued in this patient. Urticarial eruptions, easily controlled by an antihistaminic drug, occurred in three patients. Under the influence of this drug, treatment was continued with no interruption. Intracutaneous tests with crystalline penicillin failed to prove penicillin sensitivity in any one of these four patients, and it has previously been shown that pure beeswax and oil are not antigenic (29). These reactions, therefore, were presumably induced by impurities. None of them followed the use of preparations made with the pure crystalline material.

Penicillin sensitivity can occur after its use, and if a patient should develop a reaction which can be attributed to acquired sensitivity, then further treatment with P.O.B. must be discontinued in that patient.

Therefore, any case of bronchial asthma in which an infective element plays a role, deserves a trial course of P.O.B., regardless of the presence of presumed prejudicial factors such as irreversible anatomic changes (e. g. emphysema), age, long duration of symptoms or penicillin-resistance of sputum flora. It is important not to regard it as the only treatment; best results will probably be obtained by using it in conjunction with judicious symptomatic therapy.

SUMMARY

1. Previous reports on the treatment of intrinsic asthma by various methods of penicillin administration are reviewed and summarized.

2. Thirty-nine cases of intrinsic asthma treated with 600,000 units of penicillin in wax and oil daily, followed by similar booster doses every five to seven days, are reported. Thirty-one were improved.

3. It is concluded that *any* case of infective asthma deserves a trial with penicillin in wax and oil, and the majority will benefit materially.

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Caronamide: A New Enhancing Agent for Use in Conjunction With Penicillin Therapy*

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PENICILLIN that is absorbed into the circulation is excreted almost quantitatively in the urine and from 85 to 100 per cent of a given intramuscular dose can be recovered in the urine in from one to three hours. Of the amount of penicillin in the urine, 20 per cent is eliminated by glomerular filtration and 80 per cent by tubular excretion. The dominant role of the renal tubules in the rapid removal of penicillin from the body has focused attention on this portion of the nephron as a possible site at which an attack might be made on the problem of maintaining higher penicillin plasma concentrations following a stated dose of the antibiotic.

The maximal excretory capacity of the renal tubules is regularly measured by the renal physiologist with the aid of diodrast and para-aminohippuric acid, Tm_{PAH} and Tm_{D}. During the measurement of this function, it was observed originally that diodrast interfered with the excretion of penicillin (1) and later, similar observations were made with para-aminohippuric acid (2). It was thus established that, by presenting the renal tubules with a quantity of either diodrast or para-aminohippuric acid in excess of the capacity of the tubules to clear it from the plasma, the excretion of penicillin could be suppressed with elevation of penicillin plasma concentrations. The necessity of administering both diodrast and para-aminohippuric acid intravenously and in large quantities has limited the use of the compounds although both have been applied successfully to the treatment of subacute bacterial endocarditis (3, 4, 5).

* Read before the Section on General Medicine of the College of Physicians of Philadelphia, 27 October 1947.

The new compound, caronamide, is effective when administered by mouth and is capable of elevating penicillin plasma concentrations from two to seven fold by inhibiting the penicillin transport system of the renal tubules. It is becoming increasingly evident that the processes of reabsorption and secretion by the renal tubular epithelium are mediated through enzyme transport systems and it is in the light of such a system responsible for the excretion of penicillin that the action of caronamide is explained (6). A specific enzyme system is the route of elimination common to at least penicillin, diodrast, para-aminohippuric acid and phenolsulphonphthalein and this transporting mechanism can be physiologically and reversibly inhibited by caronamide. Caronamide is said to compete for a substrate essential to the functioning of the enzyme transport system and in the presence of an adequate concentration of caronamide, the system is unavailable for the transport of penicillin, or, for that matter, the transport of phenolsulphonphthalein or para-aminohippuric acid. The effectiveness of caronamide in inhibiting the excretion of penicillin, phenolsulphonphthalein and para-aminohippuric acid has been demonstrated both in laboratory animals (7, 8) and in man (9).

During the initial phases of clinical evaluation of caronamide, the work was handicapped by the lack of a suitable method for the determination of caronamide in the body fluids. The need for such a method was recognized and, in order that dosage with caronamide might be individualized, a method for determining caronamide in plasma and urine was devised (10). This method has made possible the correlation of caronamide and penicillin

plasma concentrations and a clearer definition of effective caronamide dosage.

When the method for determining caronamide in plasma and urine became available, it was of interest to discover, (a) whether the drug was rapidly absorbed, (b) whether it accumulated in the plasma following repeated administration and, (c) what plasma concentrations were required to elevate penicillin plasma concentrations. Partial answers can be given to all of these questions.

A single 4.5 Gm. dose of caronamide was administered orally to six patients and dose response curves determined by blood sampling at a half-hour, one, two and three hours respectively. The averaged results show caronamide plasma concentrations of 15 mg./100 cc. at the end of a half-hour, and 8 mg./100 cc. at the end of three hours (Table I). It is clearly indicated that the absorption of the drug is rapid and its elimination begins promptly. Prior to the availability of a method for determining caronamide in the plasma, it was observed that a 4 Gm. dose of caronamide enhanced the penicillin plasma concentrations following a constant infusion of penicillin for from five to seven hours (9). This finding was in agreement with previous work in dogs (11) that showed a positive effect of a single dose of caronamide for from four to six hours. In both dog and man, the oral dose administered represented 50 mg./kg. of body weight. Since following the 4.5 Gm. dose, the plasma concentration was only 8 mg./100 cc. at the end of three hours and an enhancement effect was noted for from five to seven hours, it is probable that caronamide plasma concentrations less than 8 mg./100 cc. partially inhibit the excretion of penicillin.

Three gram doses of caronamide were administered every three hours for twelve hours and plasma levels of caronamide were determined one hour after all doses but the first. A slow rise in the average plasma concentrations from 8 mg./100 cc. at the fourth hour to 18 mg./100 cc. at the end of thirteen hours after the beginning of the oral administration of the drug was observed (Table II). Since the question of accumulation of caronamide in the plasma is a very pertinent one, the compound was administered continuously for a longer period. Five patients were given 1.5 Gm. every three hours and five other patients were given 3.0 Gm. every three hours for a week. At the lower level of dosage the average plasma concentration of the five patients over a period of a week was 12.5 mg./100 cc. although one patient showed consistently higher levels and was the exceptional case in this group. On the higher schedule of dosage, the average concentrations was 35 mg./100 cc. and there was a tendency for the plasma concentration to rise over the period of observation (Table III). None of these patients showed any toxic symptoms but from the

TABLE I

PLASMA CONCENTRATIONS OF CARONAMIDE FOLLOWING ORAL ADMINISTRATION OF 4.5 GRAMS

PATIENT	AGE	CARONAMIDE PLASMA CONCENTRATION, MG./100 CC.				
		Time after caronamide dose				
		30 min.	1 hr.	1½ hr.	2 hr.	3 hr.
H. F.	48	7.24	9.05	8.74	9.60	11.28
L. N.	46	15.70	12.00	17.65	11.96	13.40
F. R.	46	20.26	15.88	13.90	9.04	7.38
Z. D.	26	13.20	10.28	8.32	5.73	4.20
H. M.	55	18.25	14.48	11.80	10.22	6.32
C. W.	53	18.16	18.76	23.52	18.14	14.80

TABLE II

PLASMA CONCENTRATIONS* FOLLOWING ORAL MEDICATION FOR TWELVE HOURS

PATIENT	AGE	CARONAMIDE PLASMA CONCENTRATIONS, MG./100 CC.			
		Hours after first dose of caronamide			
		4	7	10	13
P. B.	56	1 05	19.43	8.40	14.70
H. G.	64	9.98	10.50	23.10	22.10
E. H.	69	11.60	10.50	30.50	16.30
C. C.	47	8.40	—	21.00	18.40
W. C.	25	3.15	6.30	5.78	27.30
T. B.	63	—	15.20	11.60	10.50

* All determinations done on samples drawn one hour after a 3 gram oral dose of caronamide.

results of subsequent work, it can be said that some patients have vomited with plasma concentrations over 70 mg./100 cc. and from the standpoint of effectiveness of the compound, such levels are unnecessary and undesirable. The necessity of individualizing caronamide dosage in sick patients who are dehydrated, who belong to advanced age groups, or who are suspected of having low-grade renal impairment, should be emphasized.

Having established the approximate caronamide plasma concentrations that might be anticipated following a particular schedule of dosage, the effectiveness of various caronamid-doses in enhancing penicillin plasma cone centrations was determined. Comparison between penicillin dose response curves obtained on the same patients during a control period with penicillin alone and treatment periods with caronamide were made. Arbitrarily, a two-fold enhancement effect was established as the minimum requirement for a positive caronamide effect and enhancements of lesser degree were classified as failures. The results of this study permit certain generalizations. A caronamide plasma concentration of 15 mg./100 cc. approximates a critical level, below which a two-fold enhancement effect is seldom observed, while above this concentration, an enhancement effect is uniformly obtained. One striking exception has been questioned for there was reasonable doubt about the patient having received the prescribed dose of penicillin and under these circumstances, a "failure" by the standard we have set is almost certain to occur. From these same data, it may be said that plasma concentrations between 20 and 40 mg./100 cc. were obtained regularly with 3 Gm. of caronamide every three hours.

TABLE III

PLASMA CONCENTRATIONS OF CARONAMIDE FOLLOWING CONTINUOUS ORAL ADMINISTRATION

PATIENT	AGE	CARONAMIDE	WEIGHT	CARONAMIDE PLASMA CONCENTRATIONS, MG./100 CC.						
				Days of therapy						
				1	2	3	4	5	6	7
		gms./day								
R. Y.	64	12	130	5.50	8.60	6.60	11.40	3.30	—	—
J. C.	60	12	102	22.80	30.40	30.40	35.20	31.50	—	—
A. J.	59	12	161	2.08	9.08	11.60	—	9.98	5.38	6.42
J. O.	71	12	119	7.78	3.22	19.10	—	17.40	21.90	27.04
H. A.	26	12	138	2.06	1.80	2.94	—	0.52	0.00	2.08
Averages				8.04	10.62	15.40	23.30	12.50	9.10	11.84
C. P.	49	24	158	20.90	29.40	30.00	24.30	49.20	—	—
T. H.	49	24	116	31.40	48.80	36.50	47.80	58.60	—	—
P. B.	44	24	126	7.80	39.90	12.00	—	82.80	42.40	35.80
E. D.	49	24	158	0.80	20.3	7.50	—	34.89	36.90	44.90
L. N.	46	24	192	17.00	32.0	35.00	—	47.00	61.00	—
Averages				15.50	27.80	24.20	36.00	54.40	46.70	40.30

In Table III the caronamide levels that might be anticipated from a given dose of caronamide were presented and it can be seen that the critical level of 15 mg./100 cc. is slightly above the concentration that can be expected following the administration of 1.5 Gm. of caronamide every three hours. It was therefore, of interest to observe the relative effectiveness of different caronamide dosage schedules on intramuscular injections of penicillin. The results presented represent average values obtained from penicillin dose response

curves at various levels of penicillin dosage, the number of curves constituting each average is indicated (Table IV). In all instances the effect of 3 Gm. every three hours is greater than that obtained with 1.5 Gm. every three hours and these data are interpreted as indicating that the caronamide plasma concentrations resulting from the smaller dose produce partial inhibition of penicillin excretion and the larger dose produces a more nearly maximal inhibition.

The summary of these results clearly implies the therapeutic application that can be made of caronamide. Administration of 3 Gm. of caronamide every three hours elevates the penicillin plasma concentrations following 50,000 units intramuscularly to the level of those obtained following 125,000 units alone; those after 125,000 units to the usual levels anticipated after 500,000 units alone; and those after 500,000 units to levels equal to or exceeding those ordinarily obtained after the injection of 1,000,000 units of penicillin alone. At the higher dosage levels the conservation of penicillin is tremendous.

This report would not be complete without some word about the toxicity of caronamide. The toxicity manifestations following the administration of this drug have been surprisingly few. Nausea and vomiting have been observed rather frequently but a major part of this has been undoubtedly due to mechanical irritation incident to swallowing the number of

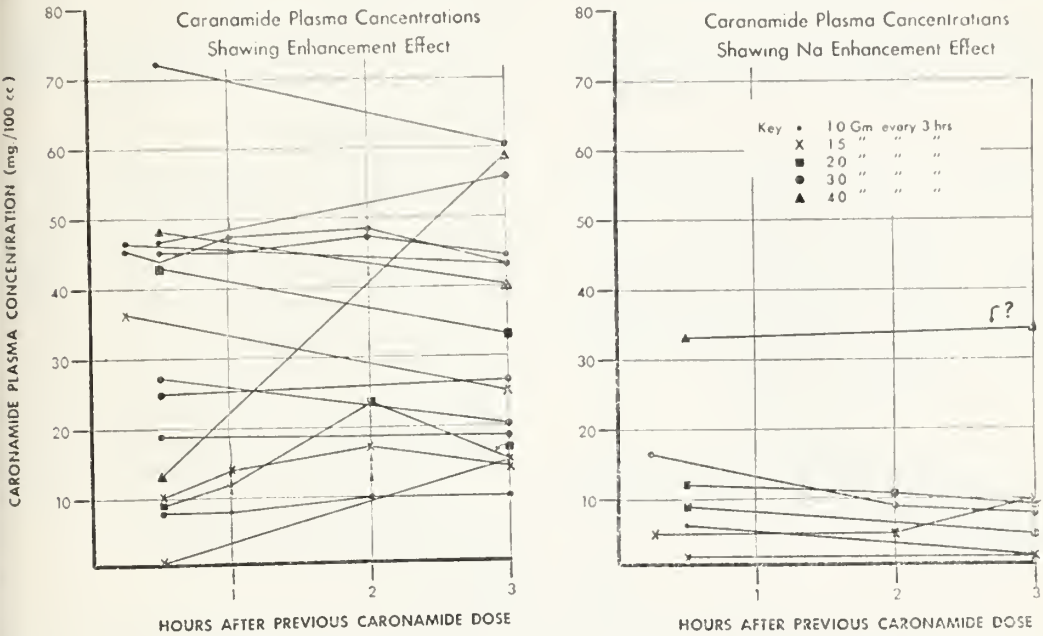
Caronamide Plasma Concentrations
Showing Enhancement Effect
CARONAMIDE PLASMA CONCENTRATION (mg./100 cc.)
HOURS AFTER PREVIOUS CARONAMIDE DOSE
Caronamide Plasma Concentrations
Showing No Enhancement Effect
Key • 10 Gm every 3 hrs
X 15 " " "
■ 20 " " "
● 30 " " "
▲ 40 " " "
HOURS AFTER PREVIOUS CARONAMIDE DOSE

FIG. 1. CORRELATION OF CARONAMIDE AND PENICILLIN PLASMA CONCENTRATIONS

TABLE IV

Effect of Oral Caronamide on Intramuscular Injections of Penicillin

Intramuscular Penicillin Dose	Caronamide Dose	Penicillin Plasma Concentrations					Patients
		15 min.	30 min.	1 hr.	2 hr.	3 hr.	
u.	*gm./3 hr.*	*units/cc.*					
125,000		3.42	3.80	1.79	.73	.25	6
125,000	2	6.82	10.86	5.33	2.00	2.75	2
125,000	3	11.53	13.87	6.91	4.15	3.40	2
200,000		5.91	3.71	2.03	.71	.23	7
200,000	2	5.84	10.65	5 84	2.78	1.75	3
200,000	3	12.22	10.21	7.50	4.53	2.74	4
250,000		8.95	7.61	3.71	1.58	.69	4
250,000	3	11.10	11.10	5.49	2.08	1.02	1
250,000	4	16.66	13.78	11.99	5.94	3.46	2
500,000		14.52	14.74	7.47	5.04	2.41	5
500,000	3	29.36	34.65	31.98	20.51	17.65	4

0.5 Gm. tablets required at higher dosage levels. This explanation is strengthened by the finding that many patients can continue at the same level of dosage without symptoms if a caronamide suspension is substituted for the tablets. Since the method for determining plasma concentrations of caronamide has become available, it has been found that at least two patients who have vomited have had plasma caronamide concentrations that exceeded 70 mg./100 cc. With a method available for determining plasma caronamide concentrations, dosage can be individualized and these excessive levels avoided. One instance of typical drug rash and fever has been observed and was proven to be due to caronamide. This drug is new and has not yet been employed widely enough to speak with finality about its toxicity but, at present, it appears to have a low order of toxicity.

CONCLUSIONS

1. Caronamide administered orally enhances penicillin plasma concentrations from two to ten times.

2. Caronamide plasma concentration of 15 mg. per 100 cc. probably is a critical level below which a two-fold enhancement effect on penicillin plasma levels cannot be regularly expected in patients with normally functioning kidneys.

3. Three grams every three hours will maintain plasma caronamide concentrations between 20–40 mg. per 100 cc. in the majority of patients, and these concentrations will produce maximal inhibition of tubular excretion of penicillin.

4. Occasionally, nausea and vomiting have been observed, most of which has been due to mechanical irritation due to swallowing the large dose of drug. Several patients have vomited with caronamide plasma concentrations above 70 mg./100 cc. and in these instances, the vomiting probably represented drug toxicity.

5. Individualization of caronamide dosage is strongly recommended and is made possible by the availability of a method for determining caronamide in the body fluids.

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Penicillin Plus Caronamide in the Treatment of Subacute Bacterial Endocarditis*

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FOLLOWING completion of the first clinical studies on caronamide, in which enhancement of penicillin blood levels was attained without accompanying toxic effects (8), we decided to use the drug in the treatment of two patients at that time in the hospital with subacute bacterial endocarditis. Both of these patients had relapsed after previous insufficient treatment with penicillin, and thus could be suspected of showing increased resistance to it (1, 5, 6, 7). At the same time we felt that the need for prolonged treatment in this disease would provide an excellent testing-ground for possible caronamide toxic effects.

We performed the following study on these patients. Bone marrow smears and cultures, and tests of renal, hepatic and hematopoietic functions were performed before, during and after the course of therapy which was as follows: 100,000 units of sodium penicillin was administered every three hours intramuscularly, and after an equilibration period, a three hour time-concentration curve was determined. At the end of this period caronamide was added, 1.5 gm. every third hour by mouth with 3 gm. as an initial dose. Another penicillin time-concentration curve was determined after an equilibration period on the combined therapy schedule. Thereafter, penicillin concentrations were taken at a standard time twice weekly during the period of combined drug administration, and a time-concentration curve was determined at the end of caronamide administration and before penicillin was stopped.

The first two cases of this report had already been started on their penicillin course when it was decided to administer caronamide.

Case I

A white male, seventeen years old, with three previous attacks of rheumatic fever, was admitted to the hospital on the 15th of November, 1946, with a tentative diagnosis of subacute bacterial endocarditis. He had received small amounts of penicillin in September and again just previous to admission.

On admission he showed physical signs of mitral and aortic valvular disease and a temperature of 99°. In addition his spleen was enlarged and tender and he showed numerous petechiae. Blood culture was positive on the 18th and 19th and showed alpha streptococci sensitive to 0.37 units/c.c. of penicillin.

Penicillin was begun at noon on November 21st. Caronamide was begun twelve days later. A peculiar macular rash was noted on the left lower forearm the day following the first administration of caronamide but disappeared within the next four days. Two transfusions of 250 c.c. of whole blood were given on the next two succeeding days.

The first temperature elevations in eighteen days were noted on the 8th and 9th of December, the temperature going to 99.8° and 100° respectively. At 4:30 a.m. on the 10th of December the patient had a shaking chill and within an hour his temperature rose to 104°. On the same afternoon a scarlet, maculopapular rash was noted on the dorsal and lateral aspects of the proximal phalanges of both hands. By the next morning this rash had become confluent along both arms and was seen on the legs, face, back and neck. Caronamide was stopped at noon of that day. During the afternoon the rash gradually as-

* Read before the Section on General Medicine of the College of Physicians of Philadelphia, 27 October 1947.

sumed urticarial characteristics, itching severely and closing his right eye. It was subsiding in two days and was completely gone in four, by which time his temperature had become normal.

Following an uneventful three days, 3 gm. of caronamide was again given at 3:00 a.m. By 4:00 a.m. he was acutely ill, nauseated and vomiting, and he had a shaking chill with temperature of 104°, pulse of 130 and respirations of 30. His lips and nail beds were cyanotic, his face and trunk were flushed and bilateral ankle and knee clonus were elicited.

Treatment consisted of intravenous infusions of glucose, saline, and sodium lactate, plus adrenalin, benadryl and calcium gluconate, ice water enemas, alcohol sponge baths, and oxygen. He continued to be listless, slightly irrational on questioning, anuric, and to show persistent, marked erythema and ankle clonus until about 10:00 p.m. when he became mentally more alert, and voided for the first time in nearly twenty-four hours. The next morning he had no complaints except for a moderate weakness. Examination disclosed weakness of the upper and lower extremity, increased tendon reflexes and clonus all on the left side. The skin erythema lessened, the output rose and by the 20th of December (three days later) the only trace of the severe reaction was a fine branny desquamation of the skin of his face.

Penicillin was stopped on 12/21/46 and the patient was discharged from the hospital on January 27th, 1947. His subsequent course to date has been uneventful (a follow-up period of nine months).

This patient's pre-drug-phase concentration curve is not characteristic of levels following a single intramuscular injection of penicillin (4). Since his other two curves follow the typical pattern, we feel that this is probably due to laboratory error. This was our first case, and at that time we were having difficulty in establishing reproducible results in plasma penicillin levels. We have no explanation for the non-characteristic behavior of the post-drug-phase concentration curve. These curves are presented solely to complete the record of the only severe reaction to caronamide that we have encountered or heard of. We cannot feel that they are accurate representations of conditions that existed.

Case II

A white female, twenty-four years of age, with a history of chorea at age twelve, was admitted to the hospital on November 22nd, 1946, with a tentative diagnosis of subacute bacterial endocarditis. She had received penicillin on the basis of other diagnoses early in October and again in November. She had had five negative blood cultures at another hospital during the preceding month.

On admission, she had a temperature of 99°, physical signs of mitral valvular disease, clubbing of the fingers and an inflamed left ankle. Blood cultures on November 23rd and November 25th showed alpha streptococcus. Penicillin sensitivity was determined at 0.15 units/c.c.

Penicillin was begun on November 27th, 1946. Blood culture on December 7th was again positive, and on December 9th caronamide was started. Because of strongly positive tests for urinary albumin caronamide was stopped on December 14th but was restarted three days later, after it was determined that the precipitate was caronamide rather than albumin. She continued to show an occasional mild fever and on the 29th of December emboli appeared in the left ring finger and palm.

All treatment was discontinued on December 31st. Blood culture taken on the 6th of January, 1947, showed an alpha streptococcus sensitive to 2.5 units/c.c. of penicillin, a greater than tenfold decrease in organism sensitivity.

Massive penicillin therapy (one million units intramuscularly every third hour and 300,000 units of Romansky formula every twelve hours) was begun on the 16th of January, 1947 and continued until the 12th of February. She was discharged from the hospital on February 26th, having gained weight and been afebrile since the 18th. Her sub-

sequent course has been uneventful over an eight month period.

The height of the post-drug-phase curve, as compared with the pre-drug-phase curve, in this patient may be explained on the basis of incomplete elimination of caronamide or on a tardiness in recovery of the renal transport mechanism following caronamide. Boger has found evidence to suggest a mechanism of this sort (2).

Case III

A white female, thirty-nine years of age, whose previous medical history contains a period of chorea at age ten and a ruptured appendix at age fifteen, followed by a fecal fistula, right empyema and rib resection. The empyema recurred following a respiratory infection at age twenty-three and rupture of a sub-diaphragmatic abscess into the right pleural space occurred six years later. She was first seen in this hospital on the 1st of November, 1946, with a diagnosis of cerebral embolism followed by hemiplegia and probable brain abscess. She improved following a month's treatment with penicillin. One positive blood culture had been obtained but sensitivity had not been determined. Follow-up examination in March revealed a palpable spleen and an Osler's node in the right fifth finger.

On re-admission, March 13th, 1947, she showed the residual findings of a left hemiplegia, a palpable spleen and a transient mitral systolic murmur. Blood culture, positive for alpha streptococci before her admission, showed, on re-culture the day of admission, an organism sensitive to 2.5 units/c.c. of penicillin.

On the 15th of March she was started on sulfadiazine, gm. 1 every four hours, which was discontinued six days later. On March the 17th, penicillin was started with 500,000 units every three hours and on the 24th caronamide was begun. Her course was uneventful except for a single Osler's node noted in her right thumb on March the 29th. Caronamide was stopped on April 12th, 1947, and penicillin on April 16th. Her subsequent course has shown steady improvement over the last six months.

This case shows a typical example of the effects of caronamide on penicillin plasma levels despite dosage of caronamide that would now be considered inadequate in the average person.

After Dr. Boger's paper† it would be pointless to discuss the theory of the mode of action of caronamide. However, at the time we were treating these cases there was no accurate method for determination of caronamide blood levels, and the concept of an "enhancement level" of caronamide, while dimly appreciated, had not yet been clarified.

DISCUSSION

We feel certain that our failure with the combined treatment in the second case was due to inadequate caronamide dosage with consequent plasma levels of penicillin lower than those required to kill the invading organism (3), and its subsequent marked decrease in penicillin sensitivity. It is unfortunate that we could not continue caronamide therapy in this patient but she refused further studies at the time she was changed to massive penicillin dosage.

With the exception of occasional nausea and vomiting, there are no other reports in the literature of toxic reactions such as we encountered in the first patient.

The third case does not properly fit within the limits of the study since her penicillin dosage was higher than that used in the other two patients. However, she exhibits the characteristic influence of caronamide on penicillin blood levels and so was included.

SUMMARY

Three cases of subacute bacterial endocarditis treated with penicillin and the adjuvant drug, caronamide, have been presented. All cases exhibited the penicillin-enhancing effect of caronamide and one showed a hitherto unen-

† See Dr. Boger's paper, which immediately precedes this one. (Ed.)

countered sensitivity to that drug. In no case was there seen any alteration in the renal, hepatic or hematopoietic functions as expressed by the tests of these functions performed during and after caronamide administration.

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Experimental Studies of the "Common Cold" in Human Volunteers*

By JOHN H. DINGLE, M.D.
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IN accepting the invitation to deliver the Anders Lecture tonight, I have chosen to speak as a representative of the group of investigators who planned and carried out the work which forms the basis of this lecture. These investigators, who were members and professional associates of the Commission on Acute Respiratory Diseases of the Army Epidemiological Board, are as follows: Doctors Theodore J. Abernethy, George F. Badger, Norman L. Cressy, A. E. Feller, Irving Gordon, Alexander D. Langmuir, Charles H. Rammelkamp, and Elias Strauss. It is a privilege to share with them in the recognition which your invitation has afforded our work.

The "common cold" is a term which is generally applied to a mild respiratory illness characterized by an acute catarrhal inflammation of the upper respiratory passages, and particularly, of the nasal mucous membranes and the contiguous structures in the sinuses. The term calls to mind the picture of a "woe-be-gone" individual whose eyes are congested and watery, whose nose is red and "running," whose voice is "nasal," who feels "mean and irritable," and who usually insists that he isn't "sick." This state of discomfort continues for 2 or 3 days. Then the symptoms and signs gradually abate, and the sufferer recovers from his "cold."

If the above picture be accurate, it should follow that recognition of the "common cold" is easy and investigation of it is a straightforward procedure. Unfortunately, such is not the case. Some "colds" extend from the nose to involve the rest of the respiratory tract, others begin in the throat or the trachea and only later involve the nose, and still others do not involve the nose at all. Some "colds" appear to be merely localized infections of a portion of the upper respiratory tract; others seem to be systemic infections which are associated with fever and constitutional symptoms and which may eventuate in pneumonia.

Thus it would appear that clinical character, istics alone are not sufficient to delimit the problem of the "common cold." Likewise-epidemiological behavior has not delineated clearly the scope of the problem. Apart from isolated communities, individual "colds" occur constantly, and epidemic waves appear at various times of the year, though with greater intensity and severity apparent during the winter months. Moreover, the illnesses during these waves do not present a uniform clinical picture.

The greatest step forward has come from etiological studies. The work of Kruse (1), Foster (2), Dochez (3), Long (4), and their co-workers has demonstrated that a coryzal type of illness can be transmitted to well

* James M. Anders Lecture XXI, College of Physicians of Philadelphia, 4 December 1946.

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The investigative work forming the basis of this lecture was supported in part through the Commission on Acute Respiratory Diseases, Board for the Investigation and Control of Influenza and Other Epidemic Diseases in the Army, Preventive Medicine Service, Office of the Surgeon General, United States Army, and by grants from the Commonwealth Fund, the W. K. Kellogg Foundation, the John and Mary R. Markle Foundation, and the International Health Division of the Rockefeller Foundation to the Board for the Investigation and Control of Influenza and Other Epidemic Diseases for the Commission on Acute Respiratory Diseases.

human beings and to chimpanzees by bacteria-free washings of the upper respiratory passages of patients with "colds." But here the problem had rested prior to the War.

During the past four years, the Commission on Acute Respiratory Diseases has studied in the Army the large group of respiratory illnesses of unknown etiology in an attempt to segregate "entities." It early became apparent that, within this group, the types of illness covered a broad span—or spectrum—from the "common cold" or mild, afebrile coryzal infections at one end, to severe primary atypical pneumonia at the other end. Prominent between these two extremes was a non-coryzal type of respiratory infection which was characterized by fever and constitutional symptoms and which occurred epidemically in recruits during the winter months. This type of illness has been termed "undifferentiated acute respiratory disease" (10). No sharp lines of demarcation were detectable clinically or epidemiologically at any place within the span and the number of possible entities within it was indeterminate. Accordingly, etiological investigation of one type of respiratory illness required collateral study of other types.

The first such etiological studies carried out by the Commission (5) in human volunteers dealt with that end of the span, or spectrum, occupied by primary atypical pneumonia. This study demonstrated that primary atypical pneumonia was transmitted to approximately one-quarter of the volunteers by pooled, bacteria-free filtrates of sputa and throat washings from cases of this disease. In addition, such pooled filtrates induced minor respiratory illnesses, without pulmonary involvement, in approximately one-half of the inoculated subjects. These results appeared to be compatible with the hypothesis (6–10) that primary atypical pneumonia might be merely a severe form, with involvement of the lungs, of a milder and more prevalent acute respiratory disease. The findings did not constitute proof of this theory, however, since the possibility of more than one virus in the pooled inocula, collected from several donors, could not be excluded.

The second study dealt with the opposite or "common cold" end of the spectrum and the types of illness lying between the two extremes. The purposes were twofold: (a) to segregate "entities" from the types of undifferentiated respiratory illness, and (b) to clarify the relation between primary atypical pneumonia and minor respiratory illnesses. To this end, human volunteers were inoculated with bacteria-free, filtered throat washings collected from 4 donor subjects whose illnesses appeared to represent clinically different types of respiratory disease. Reinoculation of the volunteers was carried out in an attempt to determine the immunological relation of the resulting illnesses to one another and to primary atypical pneumonia.

I wish to present tonight a summary of the results of this second study. A preliminary report of this work has been presented before the American Society for Clinical Investigation and a detailed report by the Commission on Acute Respiratory Diseases is appearing separately (11).

The studies were carried out under conditions designed to insure freedom of the volunteers from respiratory disease prior to their initial inoculation and to prevent cross-infection or chance exposure to respiratory disease after inoculation. Each volunteer was therefore isolated in an individual room during the experimental period. The inocula consisted of bacteria-free, filtered washings of the upper respiratory passages of the donor-subjects. Ten ml. of the respective inocula were administered by spraying the material from an atomizer and nebulizer into the nose and throat of the volunteer, in synchronization with deep inspiration. Regular and repeated clinical and laboratory observations were made throughout the period of the studies.

The results will be presented under two headings: (*1*) the production of minor respiratory illnesses and (*2*) the immunological relation of the illnesses to one another and to primary atypical pneumonia.

Production of minor respiratory illnesses. As pointed out earlier, 4 donor-subjects were selected whose illnesses appeared to represent clinically different types of respiratory disease.

The first donor (Figure 1), a recruit, suffered a moderately severe febrile illness which was termed "acute respiratory disease" or ARD. Feverishness and sore throat were the outstanding features, followed by hoarseness and cough. Nasal symptoms were minimal. Abnormal physical findings consisted of injection of the palate, pharynx and tonsils. There was no evidence of pneumonia. Laboratory examinations yielded no abnormal findings. The duration of illness was 6 days. Of the 19 volunteers inoculated with filtrate from this donor, 14 developed minor respiratory illnesses. The illnesses were mild and of somewhat varied clinical pattern, but, in general, symptoms and signs referable to the throat were characteristic, and nasal symptoms were of minimal intensity and not associated with obvious signs of nasal obstruction or discharge.

The illness in the second donor (Figure 2), a laboratory officer, was characterized by coryza, fever, and constitutional symptoms, and was termed a "severe common cold" or S-CC. Associated with the nasal symptoms were feverishness, headache, malaise, cough, and substernal soreness. The principal physical findings were edema and injection of the nasal mucosa, and, on the 3rd day, profuse serous nasal discharge. Sorethroat and pharyngeal inflammation were not present. No evidence of pneumonia was noted at any time. Laboratory studies were non-contributory. The duration of symptoms was 16 days. Of the 19 volunteers given the S-CC inoculum from this donor, 13 developed respiratory infections characterized by sneezing, nasal obstruction and objective evidence of coryza.

The third donor (Figure 3), a medical officer, experienced a mild coryzal illness, without fever, termed a "common cold" or CC. The early symptoms of irritation of the nose and of dry throat were followed by sneezing and copi-

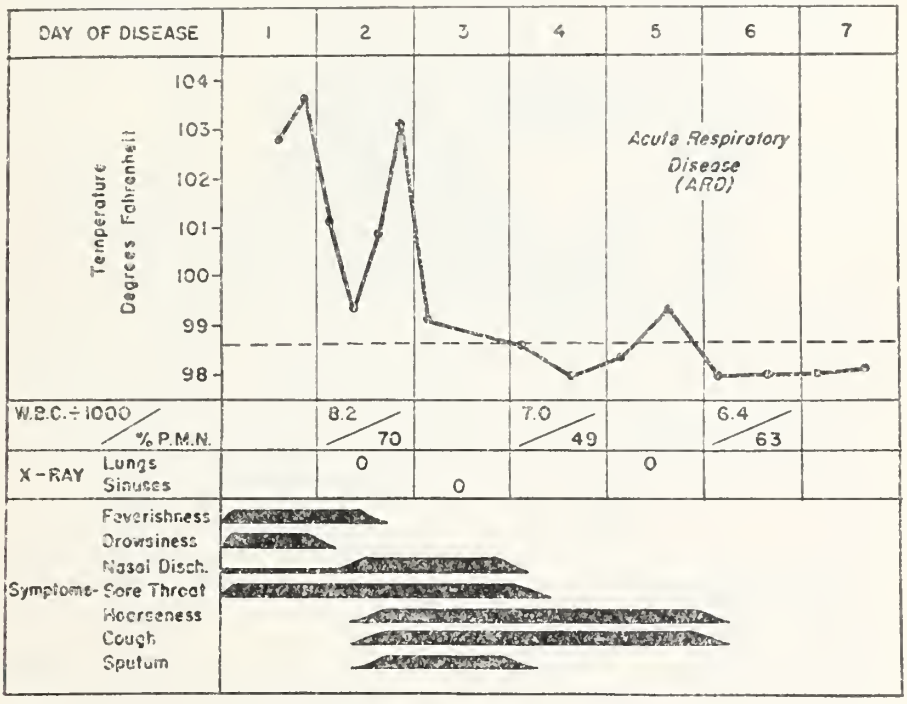

FIG. 1. CLINICAL CHART OF DONOR WHOSE ILLNESS WAS TERMED "ACUTE RESPIRATORY DISEASE" (ARD)

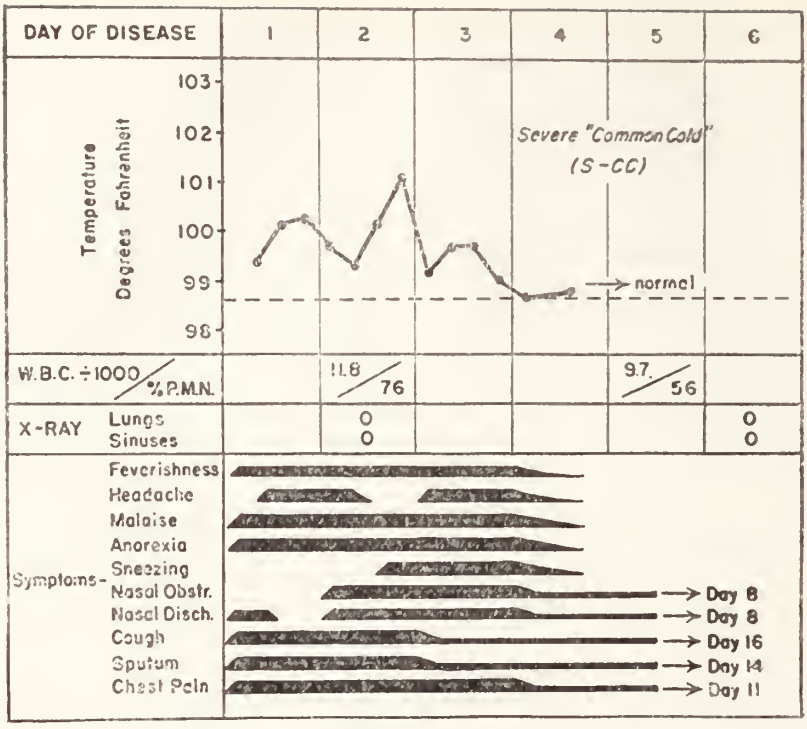

FIG. 2. CLINICAL CHART OF DONOR WHOSE ILLNESS WAS TERMED "SEVERE COMMON COLD" (S-CC)

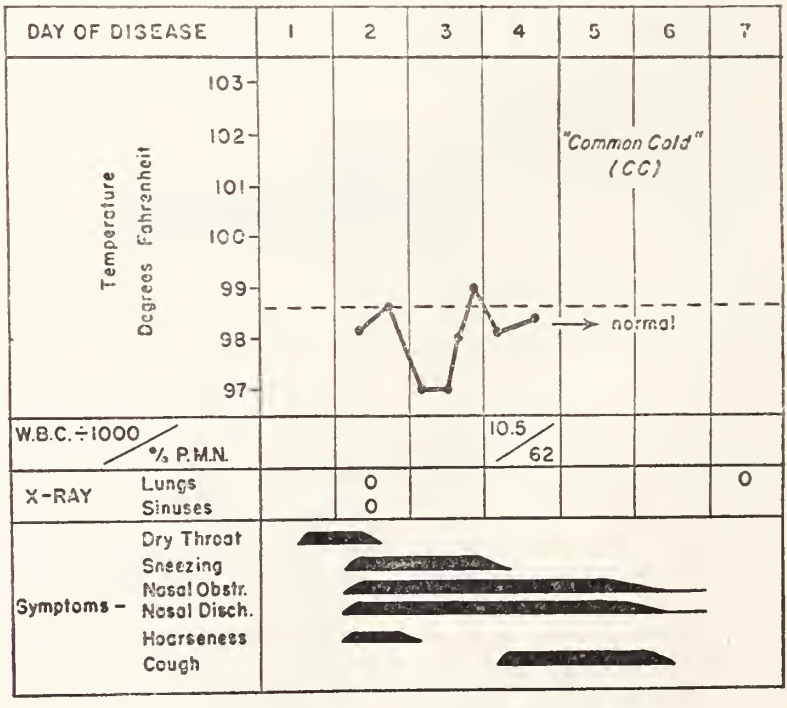

FIG. 3. CLINICAL CHART OF DONOR WHOSE ILLNESS WAS TERMED "COMMON COLD" (CC)

ous nasal discharge. Constitutional symptoms were absent. Physical findings were limited to congestion and edema of the nasal mucosa. There was no evidence of pneumonia. The duration of illness was 6 days. Six of the 10 subjects inoculated with the filtrate from this donor developed mild, afebrile illnesses characterized by sneezing, nasal obstruction and coryza.

The last donor (Figure 4), a recruit, experienced a severe febrile illness, with marked constitutional symptoms and rales in the lungs. This illness has been termed "bronchitis resembling atypical pneumonia," or Br-AP. The symptoms, physical signs, laboratory findings and course were consistent with the diagnosis of primary atypical pneumonia, but roentgenographic evidence of pulmonary infiltration was lacking. Of the 10 volunteers receiving Br-AP filtrate, 4 developed minor respiratory illnesses which were mild, afebrile, and showed no characteristic clinical pattern. There was no evidence of pulmonary involvement in any of the recipients.

As a control of the procedures and manipulations required for inoculation, 9 volunteers were inoculated with filtered specimens of their own throat washings obtained from them several days previously. Each of the 9 men remained entirely well for a period of 30 days following inoculation.

A summary of the illnesses produced with each type of inoculum is given in Table 1. It may be pointed out here, that bacteriological and serological studies on each of the donors, and likewise of the volunteers who became ill, failed to provide any evidence pointing to a diagnosis of influenza A or B, or of a bacterial infection of the respiratory tract.

The general clinical characteristics of the illnesses induced by filtrates from three of these donors suggested that two types of infection had resulted: A predominantly pharyngeal illness from the ARD filtrate, and a

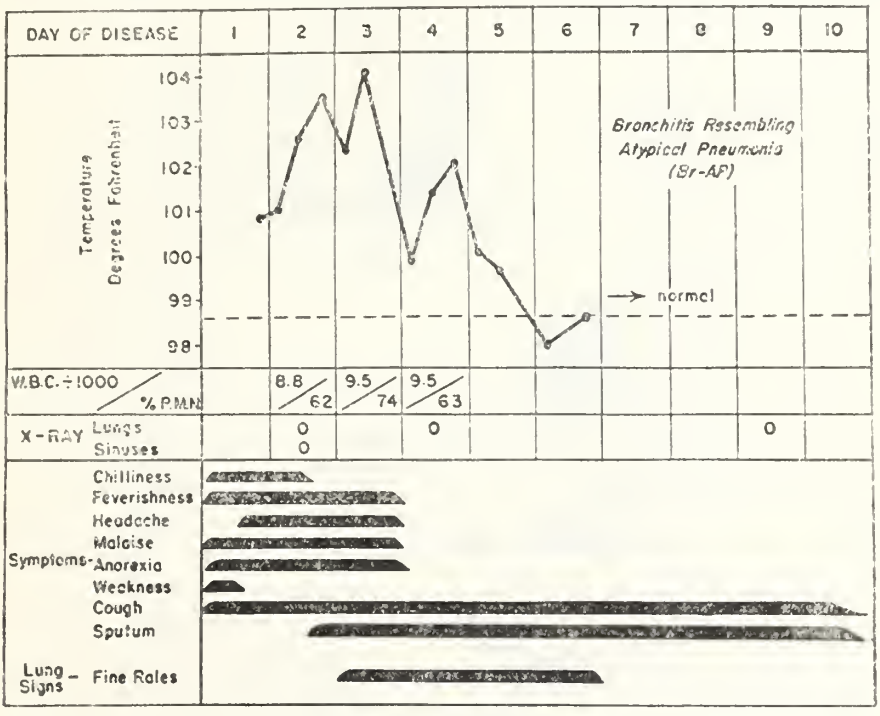

FIG. 4. CLINICAL CHART OF DONOR WHOSE ILLNESS WAS TERMED "BRONCHITIS RESEMBLING ATYPICAL PNEUMONIA" (Br-AP)

coryzal type of disease from the S-CC and CC filtrates. The illnesses following administration of the fourth or Br-AP filtrate could not adequately be characterized. Detailed analysis indicated further similarities and differences of sufficient magnitude to suggest the existence of "entities."

The most striking evidence was found in the incubation periods of the illnesses in the recipients (Figure 5). The ARD filtrate induced illness in 3 to 9 days after inoculation, but in 10 of the 14 cases onset of illness occurred on the 5th and 6th days. In contrast, the S-CC and CC filtrates induced illnesses, with a single exception, on the 1st and 2nd post-inoculation days. The incubation period of the Br-AP group is not clearly defined because of the small number of illnesses.

Analysis of the time of appearance and daily frequency of nasal and throat symptoms revealed differences between the illnesses induced by the ARD and S-CC filtrates (Figure 6). Nasal symptoms appeared earlier and in greater frequency and severity in the S-CC group than in the ARD group although little difference was noted in symptoms referable to the throat. Differences between these two groups were likewise noted with respect to the occurrence and frequency of physical signs (Figure 7).

It should be emphasized that the differences in the clinical characteristics of these two types of infection were apparent at the bedside of some, but not all, of the men in the two groups. The above analysis of the appearance and daily frequency of the symptoms and signs brings out certain group differences, and justifies the distinction between the two infections. Without knowledge of the incubation periods, however, the illnesses in a few of the volunteers in each group could not have been differentiated with certainty.

Laboratory studies failed to reveal any striking or significant differences in the ill-

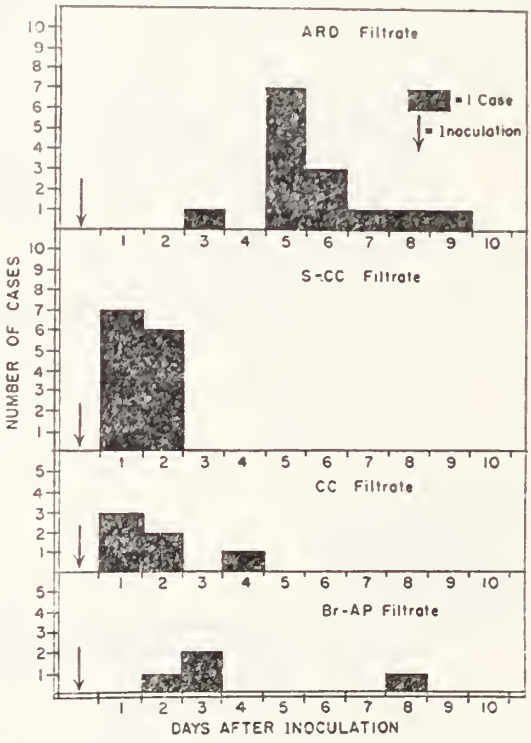

Fig. 5. Incubation Period of Minor Respiratory Illnesses in Recipients

nesses resulting from the various types of inocula.

In summary, the results of the inoculations of washings from 4 subjects whose illnesses appeared to represent clinically different types of respiratory disease led to the following tentative conclusions:

(1) On the basis of clinical characteristics and incubation periods, two types of minor respiratory illness can be differentiated: one is a coryzal or "common cold" type of infection with an incubation period of 24 to 48 hours; the other or "ARD" type, is characterized by prominence of pharyngeal involvement, minimal nasal symptoms and an incubation period of 5 to 6 days.

(2) The two types of infections appear to be due to filter-passing agents, presumably viruses, and are not the result of mechanical irritation from the inoculation procedures.

(3) Primary atypical pneumonia may be unrelated to any of the above respiratory infections in the donors or recipients, since pulmonary involvement did not occur in any of the illnesses induced by the 4 filtrates. Moreover, the incubation period of 12 to 14 days, observed previously in the experimental transmission of primary atypical pneumonia with filtered inoculum (5), is not in accord with the incubation periods observed in the present studies.

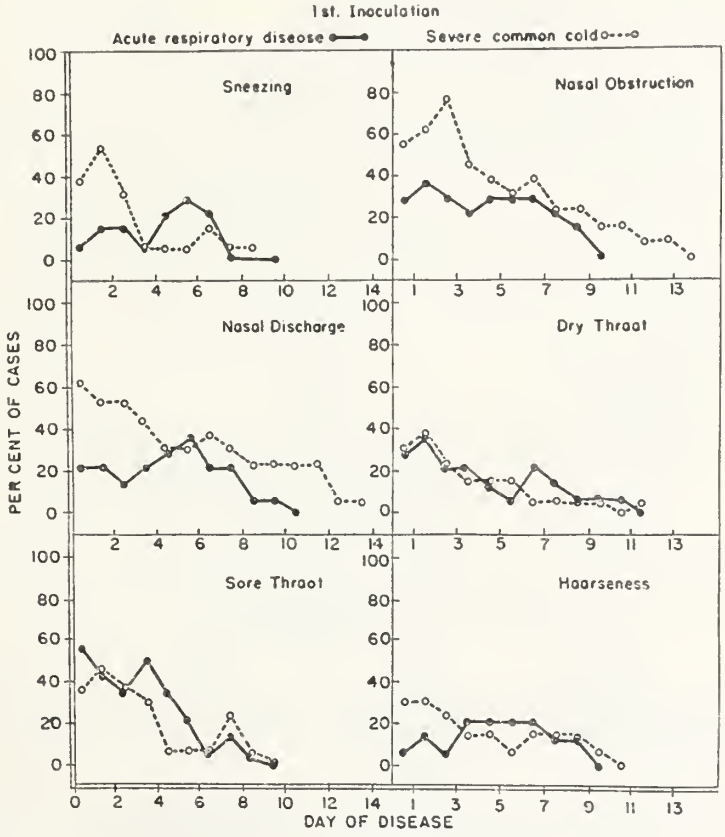

FIG. 6. PER CENT FREQUENCY OF NASAL AND THROAT SYMPTOMS BY DAY OF DISEASE

Immunological relation of the illnesses to one another and to primary atypical pneumonia. An attempt was then made to test the reliability of the above tentative conclusions by determining the presence or absence of im-

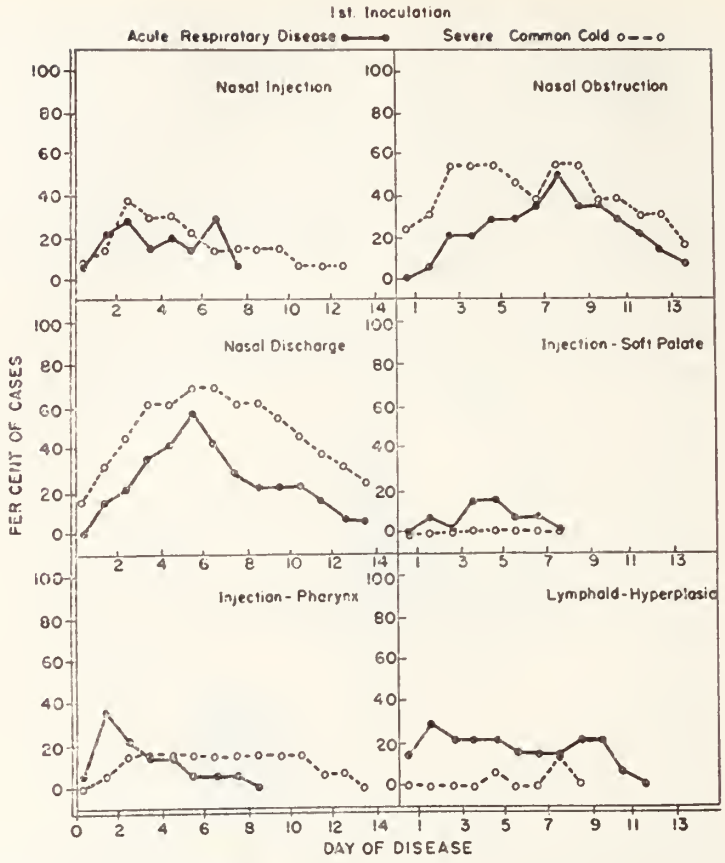

FIG. 7. PER CENT FREQUENCY OF NASAL AND THROAT SIGNS BY DAY OF DISEASE

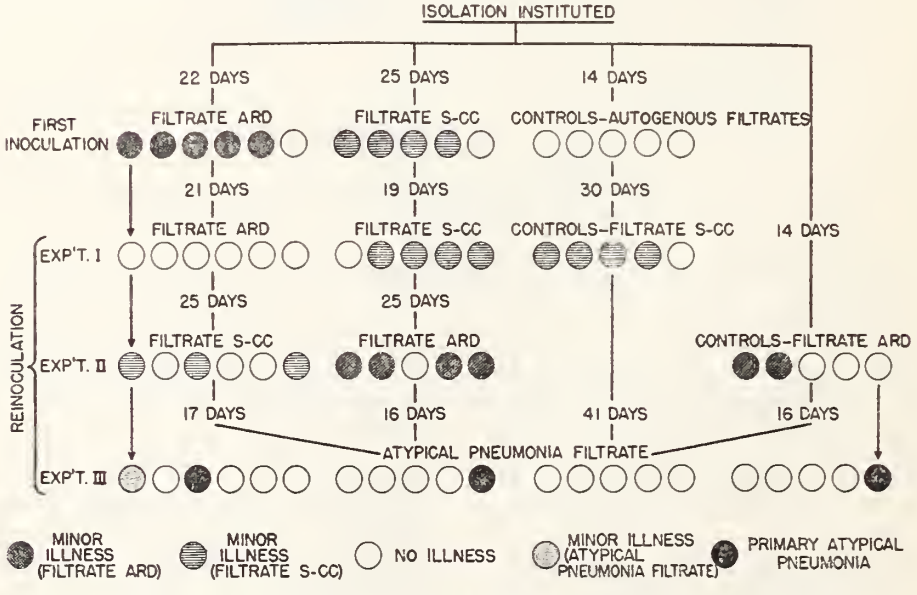

FIG. 8. RESULTS OF INOCULATION OF HOMOLOGOUS AND HETEROLOGOUS FILTRATES (EXPERIMENTS I, II, III)

munity resulting from the two types of infection, that is, the ARD, and S-CC types of illness. For this purpose some of the subjects in the initial studies agreed to remain in isolation and to be reinoculated with agents from the two types of minor respiratory illnesses and from primary atypical pneumonia. The methods outlined above were followed throughout this second portion of the study, except that dosages of certain inocula had to be reduced to 5 or 6 ml.

Three separate reinoculation experiments were carried out. In the first experiment, the subjects were given the same type of inoculum which they had initially received, in order to evaluate homologous immunity. In the second experiment, heterologous immunity was determined by administering the opposite type of inoculum, that is, by inoculating the ARD group with S-CC filtrate and contrariwise. Finally, the subjects were given filtered inoculum obtained from a patient with primary atypical pneumonia.

The results are shown in Figure 8. Each subject is represented in this chart by a circle, and the type of illness resulting from inoculation is indicated by the various degrees of shading. In the first row is shown the reaction of each man to the initial inoculation. Five of the 6 men given ARD filtrate had developed illnesses beginning 5 to 6 days after inoculation, while the sixth man had experienced no illness. Four of the 5 men inoculated with the S-CC filtrate had suffered the coryzal type of illness after an incubation period of 1 to 2 days. The 5 men given autogenous filtrates for purposes of control had experienced no illness.

Approximately three weeks after the initial inoculations, the ARD and S-CC groups of subjects were challenged with homologous filtrates (Experiment 1, second row of circles). Filtrate S-CC was administered to the control group. None of the 6 men reinoculated with the ARD filtrate became ill. In contrast, 4 of the 5 men, receiving S-CC filtrate for the second time, again became ill, as did 4 of the 5 control subjects. The illnesses experienced by these men were characteristic of those previously induced by the S-CC filtrate: coryza was the prominent feature and the incubation period was 1 to 2 days. Clinically the infections were somewhat milder in those men who had previously been ill.

Twenty-five days later the men in the two experimental groups were given the second re-inoculation (Experiment II, Figure 8). The 6 men, who had received the ARD filtrate on two occasions, were inoculated with the S-CC filtrate. ARD filtrate was administered to the 5 men previously exposed twice to the S-CC filtrate. A control group of 5 men was inoculated with the ARD filtrate. The results demonstrated a lack of heterologous immunity: 3 of the 6 men inoculated with the S-CC filtrate and 4 of the 5 men given the ARD filtrate developed respiratory illnesses. Two of the 5 men in the control group became ill. The clinical characteristics of the illnesses and the incubation periods were consistent with those previously observed with the two types of inocula.

TABLE I

SUMMARY OF RESULTS IN 58 VOLUNTEERS INOCULATED WITH FILTRATES FROM CASES OF RESPIRATORY DISEASE AND IN 9 CONTROLS INOCULATED WITH AUTOGENOUS FILTRATES

TYPE OF INOCULUM*	NUMBER OF MEN	RESULTS	
		MRI**	No illness
ARD	19	14	5
S-CC	19	13	6
CC	10	6	4
Br-AP	10	4	6
Control	9	0	9

* See text for description of terms used.
** MRI—Minor Respiratory Illness.

These experiments thus supported the tentative conclusions that the two filtrates produced two types of respiratory illness which were separate and unrelated entities. With the dosages of inocula employed, the ARD type of infection, characterized by prominence of pharyngeal symptoms and the longer incubation period, was followed by homologous immunity but not by immunity

to the heterologous S-CC or coryzal type of infection. In contrast, the S-CC or coryzal disease failed to induce solid active immunity either to itself or to the heterologous ARD infection. The control groups demonstrated that both filtrates were infectious.

In the final experiment, the 21 men were inoculated with filtered throat washings and sputum collected from a single donor in the early stage of primary atypical pneumonia. Three cases of primary atypical pneumonia and one of minor respiratory illness resulted (Experiment III, Figure 8). The three cases of pneumonia were characteristic of the naturally-acquired disease, as well as of the experimentally-induced infections (5, 9), except that cold hemagglutinins did not appear in their convalescent-phase sera. The incubation periods were 13, 14 and 15 days, respectively. Two of the 3 cases occurred in men who had previously experienced respiratory illnesses following inoculations with both the ARD and S-CC filtrates. The one patient with minor respiratory illness developed symptoms 10 days after inoculation. His illness was characterized by headache, malaise, coryza, cough and substernal chest pain. No abnormal physical findings were noted in the chest, nor was pulmonary infiltration demonstrable roentgenographically. The patient described his illness as a "chest cold" in contrast to the "head cold" he had developed following administration of the S-CC filtrate.

The results of this last experiment indicate that minor respiratory illness induced by the ARD and S-CC filtrates did not provide immunity to primary atypical pneumonia. Allowing for variations in susceptibility, the number of cases of primary atypical pneumonia which developed was consistent with the expected occurrence, based on previous studies (5). Such was not the case, however, with respect to minor respiratory illness. In the earlier studies, employing pooled filtrates from several cases of primary atypical pneumonia, approximately half of the volunteers had developed minor respiratory illness. In the present experiment, using a filtrate from a single donor, only one such case occurred. Interpretation of this result is difficult, if not impossible, because previously uninoculated control subjects were not available. It must be kept in mind that more than one virus may cause primary atypical pneumonia, and furthermore, that more than one agent may have been present in the filtrates employed in these and the earlier studies.

Considering the above studies in human volunteers in relation to the broad aspects of the problem of undifferentiated respiratory diseases, it would appear that 3 entities can now be segregated from the clinical spectrum of this group of diseases. These are (*1*) the "common cold", (*2*) acute respiratory disease (ARD), and (*3*) primary atypical pneumonia. Two of these types of illness, namely the "common cold" and "primary atypical pneumonia" lie at extreme and opposite ends of the spectrum; the third, "acute respiratory disease," lies midway between them. Each of these entities may be induced in human beings by a filter-passing agent, presumably a virus, which appears to be unrelated to the other two agents. Moreover, each entity has certain outstanding clinical characteristics which are recognizable in groups of patients, but may not be distinguishable in an individual case.

The transmission of a coryzal-type of illness with an incubation period of one or two days is in confirmation of the earlier work of Kruse (1), Foster (2), Dochez (3), Long (4), and their coworkers. The characteristics of the illnesses induced in these separate investigations appear to be similar and to be compatible with the clinical syndrome termed the "common cold." Obviously it cannot be determined at the present time whether or not the causative agents in these various experiments were the same or different. The present studies extend the previous observations, however, by demonstrating that the agent employed apparently did not induce solid immunity to itself, nor did it prevent the subsequent development of "acute respiratory disease" and of primary atypical pneumonia.

The respiratory illness transmitted by the

ARD filtrate appears to constitute a new entity, not previously induced experimentally in man. It is characterized by an incubation period of approximately 5 to 6 days, prominence of pharyngeal symptoms and signs, and the development of solid homologous immunity. Protection against the "common cold" and primary atypical pneumonia, however, was not brought about by exposure to or infection with this agent. This disease may be the same as the non-coryzal respiratory infection observed in Army recruits and termed "undifferentiated acute respiratory disease (10).

The relation between the milder respiratory illnesses and primary atypical pneumonia cannot be conclusively defined from the results of these studies in human volunteers. It would appear, however, that primary atypical pneumonia is distinct from the types of minor respiratory disease differentiated in these experiments. Pneumonia was not induced by any of the 4 filtrates employed in the study, despite the fact that the illnesses in two of the donors, namely those termed "acute respiratory disease" (ARD) and "bronchitis resembling atypical pneumonia" (Br-AP), were considered clinically to be most closely related to primary atypical pneumonia. The incubation periods of the illnesses provided another differentiating feature: that of the CC filtrate was 1 to 2 days, that of the ARD filtrate was 5 to 6 days, and that of the AP filtrate was approximately 14 days. Finally, immunity to primary atypical pneumonia did not follow infection with the agents of the "common cold" and "acute respiratory disease." Further investigation is obviously necessary to determine with certainty whether or not the agent or agents causing primary atypical pneumonia can also cause minor respiratory illness.

In conclusion, these studies indicate that two types of respiratory illness—the "common cold" and an infection which has been termed "acute respiratory disease"—can be segregated experimentally from the large group of undifferentiated respiratory diseases and from primary atypical pneumonia. This work, however, provides only a small advance toward the solution of an extraordinarily difficult problem—a problem of tremendous importance in terms of human suffering and economic loss. It is to be hoped that the relatively near future will see the full differentiation and characterization of the agents responsible for minor respiratory illnesses and the development of effective measures for prevention and control.

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The Researcher, the Searcher, and Research*

By W.B. McDANIEL, 2D
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NOT long ago I attended a meeting at which one of the speakers went to rather bizarre lengths, as it seemed to me, in defining the services she thought librarians—whom we may properly call searchers—should render unto their Caesars, the researchers. It was not only the types of service that made my eyes become increasingly exophthalmic, but the aura of sanctity, infallibility, that she managed to drape around the idols' shoulders. Listening to her, one would think they were phosphorescent in the dark. I am not *certain* that she said—but she may have—that her staff were trained to black the boots of the researcher the moment he came in the door, straighten his tie, do a double somersault, come up smiling, and gurgle, "What bit of literary 'legwork' can I do for you today, sir?"

I confess that I find something a little trying in the concept of the researcher-searcher relationship that I have just so blithely labeled. This vital relationship seems to me to ask for a more rounded consideration than the concept suggests. Not so much in the interest of the searcher and the researcher as in that of research itself. Unfortunately, what follows is in its way as fantastic as the concept which I have used as strawman. But

> "Two meanings have our lightest fantasies,—
> One of the flesh, and of the spirit one."

"I hate definitions", says a character in one of not Oscar Wilde's but Disraeli's novels—doubtless one of those characters who never discovered that dictionaries are the greatest force for law and order in the world, and very good company, to boot.

I shall define a researcher as the dweller in the ivory tower. He is the male animal. He is "Life with Father." He wears a white coat and does odd things to mice, recording what he does on graphs and charts of an Einsteinian simplicity, with microphotographs, and usually with a few ill-chosen words. He has been odd since childhood. When they could find him at all he was studiously pulling the wings off butterflies, fashioning a radio out of unlikely objects, feeding the hens spinach, experimenting with inflammable chemicals in the snug warmth and solitude of the cellar. He was something of a problem at school, because, while he was above average in the subjects that appealed to him, proficiency in more than these subjects was needed for an orderly progress up the educational ladder. He was required, for instance, to read books dealing with strange people in strange lands and he wasn't very much interested in people and still less in other lands. He was required to describe what he had seen and thought. He didn't see very much and he didn't think very much above the level of superficial action and his primary interests; for words he had little use, since his needs of communication were modest and there is a natural as well as an artificial phenomenon called Basic English. But the spirit of the time was on his side and he pulled through all right.

When he grew up he found a ready-made world of specialization, which suited him well. Now he was able to grind in and learn more and more about less and less. There was always somebody around to help him maintain contact with the outer world—eventually,

* An address delivered at the annual dinner of the Association of Honorary Consultants to the Army Medical Library, Washington, D. C., 10 October 1947; based on papers read before the Washington, D. C., Chapter of the Biological Sciences Group of the Special Libraries Association, 16 October 1945, and the New York Academy of Medicine's Institute on Libraries, 12 March 1947.

of course, this comes to be his lowly bride, the searcher—your librarian, let us say.

How shall we define a librarian? Well, the librarian, first, is the one who is expected to know all the answers; or, let me say, to have an answer to any conceivable question. He is the female animal. He is "Life with Mother" (the managing kind). (This is very confusing, I know, but I am sticking by English A as long as I can hold out.) He is often a little scatterbrained, perhaps, almost always overworked, trying desperately hard to please, usually making something out of nothing (and often nothing out of something), being told little and therefore knowing little, asking little and giving much.

Though librarianship, as we are familiar with it, is a relatively recent profession, its technical standards have already reached a very high level. (As in most professions, these standards are a good deal nearer perfect than is the general observance of them, of course.) The cultural standards of librarianship have improved rather more slowly than the technical ones, and that brings us back to the definition of the lowly bride, the searcher. Librarians today are of two classes: (1) those who just 'growed'; and (2) those, of the younger generation, who, for varying reasons, in cold blood chose to be librarians, underwent professional training, and have a diploma or certificate to prove it.

I do not propose to discuss the merits of the two classes—the individual factor is, after all, the x-factor of success in any profession. But they do have one thing, at least, in common, and in common with those of us who were educated in this country in the 20th century: they have too little of the cultural and subject background properly to be demanded by a special library that is making its full contribution to its sponsors and to the community. The B. A. and B. S. degrees, and the library school diploma, certainly the more advanced degrees, may suggest to the awestruck that the holder can read and write his own language accurately, can manipulate the major foreign languages adequately, has an interested, if superficial, knowledge of the great cultural, scientific, and social movements going on around him; but the suggestion is, alas, not always borne out by the facts.

Here then is the bridal pair: co-educated through the College level, at best, in a system which has increasingly slighted the cultural standards of citizenship, the researcher has refined his interests to a point where cultivation, appreciation, and even understanding of cultural standards has markedly deteriorated; while the searcher, not too well equipped with these in the beginning, attempts to hold and use what she has, but too often, alas, becomes hopelessly enmeshed in the complicated routines of the modern library. Being a good *Frau*, this searcher-bride tries to understand the technical details of her spouse's work, but she is endlessly harassed by routine details, and he is an impatient teacher; eventually, she becomes so adept at putting two and two together that each comes to be reconciled to a marriage that, if not made in heaven, at least works as tolerably well as most marriages do. But it is a little like the blind leading the blind—the outcome is not certain, nor is the progress as efficient and expeditious as it might be.

The late George Vaillant, director of the University of Pennsylvania Museum, once wrote: "It is a natural human failing to try to get some one else to do his legwork. Likewise it is human to take one's own field of research as the center of the universe, but librarians are human too." They are not only human but criminal, I propose, because their humanness takes the form of encouraging the human failings of the one group of workers who should be encouraged not to have any—the researchers. On them rests the hope of the world.

This "legwork" is really the villain in the piece, I think. What is it? Theoretically, it is the performance of menial tasks that any menial can safely be entrusted to perform as well as the boss-man could. That is all very well; there are such tasks. But are they

always properly recognized? The trouble is, that "legwork", as currently practiced in our country, has come to include a great deal of work that properly belongs, in my opinion, to the researcher himself. Take the matter of searching the literature. Take it, if you will, in dialogue form:

"Is it possible for the data desired by the researcher not to be neatly packaged and clearly labeled, 'For the use of whoever happens to be interested in this minute point of this large and complicated subject?' "

"Oh, yes; some of the data may well be tucked away in unexpected places."

"But the possibility of their being there would of course immediately occur to the searcher?"

"Yes; the researcher, knowing his subject and its interrelationships, would naturally immediately think of all possibilities."

"But the *searcher*, I said—the legworker. Would he?"

"Well, the researcher would have indicated carefully just what he was looking for and explained all the possible tangential headings under which it might be found."

"Hm!" (as Commander Winchell would say). "And if, by any chance, he didn't take such pains?"

"Then I suppose he might be out of luck."

"Might miss something important, you mean? Something which might have saved him embarrassment and his sponsors possibly a good deal of money?"

"Say—what do we pay our librarian-searcher for?"

What I am quarreling with, obviously, is the whole concept of research in this country and not the very human and lovable researcher or his equally human and lovable lowly bride, the librarian-searcher. That concept, unfortunately, is inextricably entangled in our generally adolescent attitude toward scholarship as such. It is our national Achilles' heel.

We make a fetish of efficiency, and yet, in this respect, we are the most inefficient people in the world, duplicating work already done, slowing up or ill-doing other work, all because of this unnatural, illogical, schizophrenic division of the work of research. In a recent report on *Biological Abstracts*, the editor-in-chief, John E. Flynn, has this to say: "One cannot follow the literature of biology for any length of time without realizing how often funds and effort are wasted and investigations delayed, because of inadequate knowledge of information already in print. Economy and efficiency of research requires that unnecessary duplication of effort, resulting from lack of information regarding what has already been accomplished, should be minimized." Of course my neighbor Flynn's panacea is bigger and better abstracting services. I am venturing to question whether the bigger and better abstracting services, which are clearly needed, might not profitably figure more prominently in the researcher's concept of his own research obligations.

The sad fact is, I think, that the researcher, happily pickled in the center of his own little universe, fully discharging his responsibilities toward the scientific conduct of his laboratory, but untrained to evaluate his work economically in terms of its historical relationships, is too often inclined to view the literature rather as a necessary evil unworthy of his personal attention—except, perhaps, when it comes to a matter of priority.

Before embarking on the investigation, he thinks, it is well to have some idea of what has been done on the subject—give the searcher a rough idea of what is in mind and have him prepare a bibliography, checking what seem to be the most substantial items. A snag arises in the course of the investigation—get the searcher to track down that point in the literature. Now we are ready to publish. I will see that our own technical procedures are set forth accurately, while the searcher checks for accuracy the sources we have quoted. I will choose the cuts, write the legends, and dictate the text, throwing in a little historical summary at the beginning based on the searcher's bibliography. The organization editor, the journal editor, the

librarian, or my secretary—somebody, anyway —will fix up the grammar a bit. The bibliography won't need to be checked again, because the librarian did it. (I hope, though, that she doesn't make another slip that will bring that fuss Van Smart down on my head again; she's usually pretty careful.) When the proof comes, it is just a matter of having the copy read back to me and making a change or two in the light of our more recent studies or of work the searcher has called to my attention since this went to press. And, oh, yes, I mustn't forget in the last paragraph of the preface, when we work this up into a book, to thank my secretary and the librarian for their painstaking efforts in typing, preparing the bibliography and in many other little ways, without which, and the patient devotion of my wife, this book could never have been written.

What is the answer? (Because, unlike the *Lancet's* recent fairy tale on the Rh Factor*, this is not intended as a dissertation on how to be happy though negative.) I think the answer is taking shape in the mood of self-inquiry engendered in all of us by the complacency-shattering events of the past decade. All are disturbed by the Frankenstein monster that science, left to its own devices, has created. Powerful movements are under way to bring the facts and the meaning of science to the people. But I hear very little of any comparable and equally important movement to bring the facts and the meaning of the humanities to the world of science. And there must be not greater fission but greater fusion of science and the humanities, if there is ever again to be peace on earth and good will among men. We have largely lost the arts of reading and listening accurately and of thinking logically. We must recapture them—if it is too late for ourselves, then for our children, through insistence on liberal, disciplined education, in which specialization follows well after the cultural demands of informed citizenship.

Translated into terms of scientific research dependent on search and analysis of the literature, this would mean, I think, the gradual development of a new race of researchers and searchers. The researcher would no longer regard the literature-aspects of his work as "legwork" pure and simple. He would view them in their economic and historical perspectives and be better equipped culturally to make economic use of them. The searcher, in turn, likewise better equipped culturally, would be trained to perform the functions of a true partner in a planned-for partnership. Then, forsooth, the marriage would no longer be one existing chiefly through mutual tolerance but one solidly grounded in knowledge exchanged and aims understood and shared in common.

"Two meanings have our lightest fantasies,—
One of the flesh, and of the spirit one."

* Since this paper went to press, the *Journal of the American Medical Association* 135: adv. p. 46, 29 Nov. 1947, has reprinted this notable example of the happily indestructible British wit.

Catalogue of the Mütter Museum of the College of Physicians of Philadelphia

Part II*

MORBID ANATOMY

1. Bones and Joints

Section 1

A. Bone Fractures
   1. Single
   2. Multiple

B. Luxations
C. Diseases
D. Pathological Changes

A. Bone Fractures

A. 1. Single

Occipital bone

—healed. 1151.08; 1151.36. B.
—ununited
  —artificial. 1151.43. A 7.
  —depressed. 1151.38. B.
  —fissured. 1151.03. B.
  —stellate. 1151.33. B.
  —gunshot
    —stellate. 1111.170, CCC. A 55.
    —perforating. 1111.122, CCC; 111.132, CCC. A 55.

Parietal bone

—healed externally; narrow unnited line inside. 1151.19. A 15.
  —depressed. 1151.32; 1151.39; 1151.49; 8600 (M). A 12; A 16; A 51.
    —without fracture. 1151.14. A 15.
—ununited. 1151.205; 1151.46. A 12.
  —compound, comminuted and depressed. 1151.35. A 51.
  —depressed. 1151.11; 1151.13; 1151.16; 1151.17. A 15.
    —with separation of sutures. 1151.12.
  —fissured. 1151.48. A 12.
  —from new-born child. 1151.20. A 15.
  —punctured; three openings. 1151.07. A 15.
  —gunshot. 1111.120, CCC; 1111.124, CCC. A 55.
    —stellate. 1111.136, CCC. A 55.

Frontal bone

—ununited
  —depressed. 1008.66; 1151.18; 1006.74. A 14; A 15.
    —of inner table only. 1151.15. A 15.
  —depressed, compound and comminuted. 1151.34. B.
  —gunshot
    —fissured. 1151.24; 1111.134, CCC. A 16; A 55.
    —radiating linear. 1111.138, CCC. A 55.

Temporal bone

—ununited; fissured, of squamous portion. 1151.28. B.
  —gunshot; small irregular hole. 1111.162, CCC. A 55.

Small portion of skull

—gunshot; depressed. 1151.51. A 55.

Malar bone

—united incompletely. 1169.08. B.

Nasal bones

—united. 1169.11. A 16.

* Part I was published in the *Transactions & Studies of the College of Physicians of Philadelphia*, vol. 15, pp. 74–89, June, 1947. Reprints of the parts, as published, are obtainable from the Curator of the Mütter Museum.

—transverse. 1169.04 to 1169.07 inclusive. A 15.

Mandible

—united. 1169.14; 1169.15; 1169.19 (1a); 1008.69, C-57; 1008.70, C-56. B; A 14; A 16.
—artificial. 1169.18. B.
—ununited. 1169.13; 1169.16; 1169.22. B; A 15.
—oblique. 1169.17; 1169.21. B.

Cervical vertebrae

—united. 17830.74.
—ununited. 1183.05; 1188.00. B.

Dorsal vertebrae

—ununited
—crushed. 17830.73; 1188.30. B.
—fissured. 1188.40. A 15.
—gunshot. 1111.210, CCC to 1111.214, CCC, inclusive. A 55.

Lumbar vertebrae

—ununited
—gunshot. 1111.230, CCC to 111.233, CCC inclusive; 1111.235, CCC. A 55.
—comminuted. 1111.234, CCC. A 55.

Sternum

—united. 1145.50. B.
—oblique. 1202.00 (1b). A 15.
—transverse. 1202.10. B.
—gunshot; depressed. 1111.325. A 55

Ribs

—united. 1217.00; 1217.02; 1217.04; 1217.06; 1217.14; 1217.18; 1217.24; 1217.26; 1217.28; 1217.30; 1217.32; 1217.37; 1217.38; 1217.41; 1217.42; 1217.44; 1217.48; 1217.50; 1217.54. B; A 15; A 16.
—with deformity. 1217.08; 1217.16; 1217.34; 1217.36. A 15.
—double. 1217.10; 1217.12; 1217.46. A 15; A 16.
—oblique. 1217.20; 1217.22; 1217.39; 1217.40. A; A 15.
—ununited. 1217.52; 1192.50; 8622 (M). B; A 12.
—gunshot. 1111.300, CCC. A 55.

Clavicle

—united. 8601 (M); 8602 (M); 8627 (M); 1232.06; 1232.08; 1232.09; 1232.10; 1232.12; 1232.14; 1232.18; 1232.20; 1232.22; 1232.24; 1232.28; 1232.30; 1232.32; 1232.34; 1232.36; 1232.40; 1232.42; 1232.44; 1232.46; 1232.48; 1232.50; 1232.56; 1232.58; with deformity. 1232.60. B; A 7; A 12; A 15; A 16.
—oblique. 1232.04; 1232.52; 1232.54; with deformity. 1232.38. B; A 12.
—comminuted. 1232.16. B.
—ununited. 1232.26; 8625 (M). B.
—occurred from disintegration due to caries. 1237.25. A 15.
—comminuted. 1232.01. B.
—gunshot. 1111.350, CCC. A 55.

Scapula

—united
—comminuted. 1247.40. B.
—stellate. 1247.00. A 15.
—ununited. 1247.10; 1247.50. A.
—transverse. 1247.30 (M). A.
—gunshot. 1111.375, CCC; 1111.376, CCC. A 55.

Humerus

—at the anatomical neck
—united. 1262.101; with eburnation. 1262.20. B; A 12.
—ununited. 1262.00. B.
—at the surgical neck
—united. 1247.05; 1262.15; 1262.26. B; A 15. A 19.
—impacted. 1262.10. A 15.
—at the greater tuberosity
—united. 1262.30. B.
—at the shaft
—united. 1262.35; 1262.56; 1262.58; 1262.72; 1262.991; with ankylosis of the elbow-joint. 1262.97; with deformity. 1262.66; 1262.68. B; A 7; A 15.
—comminuted. 1262.54 (M); 1262.94 (M). B.
—oblique. 1262.45; 1262.50; 1262.60; 1262.62; 1262.64; 1262.70. B; A 15.
—gunshot, partially united. 1111.406, CCC. A 55.
—ununited. 1268 10. A 7.
—transverse. 1262.40; 1307.00 (2a). B; A 62.
—oblique, 1262.52; 1262.93. A 15.

—gunshot. 1111.400, CCC; 1262.96; 1262.100. B; A 12; A 55.
—with necrosis. 1111.404, CCC. A 55.
—comminuted. 1262.79 A; 1262.79 B; 1262.86; 1262.87; 1262.88; 1262.90. A 54.
—transverse. 1111.410, CCC. A 55.
—at the head
—ununited; gunshot. 1262.81. A 54.
—condyle and trochlea
—united. 1262.78; 1262.80; 1262.98; with deformity. 1262.74. B; A 15.
—transverse. 1262.84. A 15.
—with ankylosis of the elbow-joint. 1262.82. B.
—ununited. 1274.10; 1262.95. B; A 12.
—resulting in separation of the epiphysis. 1262.25. B.
—gunshot; gutter. 1111.408, CCC. A 54.

Radius

—at the shaft
—united. 8607.10 (M) (3a): 8607.20 (M) (3b); 8607.30. A 37.
—ankylosis with the ulna. 1277.00. B.
—oblique. 1277.24; 1277.25; 1277.30; 1277.65. B; A 7; A 15.
—transverse. 1277.35; 1277.55; 1277.60. B; A 15.
—Colles'. 1277.40. A.
—Barton's. 1277.70. B.
—ununited; gunshot. 1277.05. A 54.
—at the neck
—united. 1277.10; A 15.
—double. 1277.20. B.
—oblique. 1277.15. B.

Ulna

—united. 1292.15; 1292.25; 1292.31. A 15; A 24.
—transverse. 1292.35. A 15.
—oblique. 1292.20; 1292.30. B; A 15.
—ununited. 1292.40; 1292.45. A 12.

Phalanges

—united; gunshot; with ankylosis. 1111.610, CCC. A 55.

Pelvis

—gunshot. 1382.15. A 54.

Innominate bone

—united; crest of ilium. 1382.50. B.
—ununited
—both ischii and pubis. 1382.30; 1382.40; 1382.45. B; A 16.
multiple. 1382.00. B.
—of ilium. 1382.08.
—comminuted, of ilium. 1382.10 (1c). A 15.
—of acetabulum and pubis. 1382.48. A 19.
—fissured (acetabulum). 1382.52. A 16.
—gunshot. 1111.702, CCC; 1111.704, CCC. A 55.
—of the ilium. 1111.724, CCC. A 55.
—comminuted; ramus pubis. 1111.720, CCC; 1111.722, CCC. A 55.

Sacrum

—united with deformity. 1188.45. A 15.
—ununited
—gunshot. 1111.750, CCC. A 55.
—lamina of first sacral vertebrae. 1111.776, CCC. A 55.
—loss of sacral spines. 1111.778, CCC. A 55.
—comminuted. 1111.780, CCC. A 55.

Leg

—deformity after fracture. 8720 (M); 8722 (M); 8723 (M).

Femur

—at the head
—ununited
—intracapsular. 1397.0035. A 66.
—gunshot. 1111.718, CCC. A 55.
—at the neck
—united. 8628 (M); 8630 (M); 8633 (M); 8634 (M); 1397.0171 (M); 1397.063 (M); 1397.10. B; A 12.
—impacted. 1397.007 (M) (4a); 1397.023. A 37.
—intracapsular. 1397.021; 1397.027. A 15.

—oblique. 1397.0255. A 19.
—transverse. 1397.0151. A 15.
—ununited. 1397.015; 1397.036. A 15.
—intracapsular. 1397.00; 1397.002; 1397.0025; 1397.003; 1397.004; 1397.0065. B; A 19; A 47; A 64; A 65.
—gunshot. 1111.806, CCC. A 55.
—transverse. 1397.001. B.
—at the head and neck
—ununited; eburnated. 1397.018.
—at the trochanters
—united. 1397.008; 1397.0321; 1397.042; with deformity. 1397.026. A 15; A 19.
—oblique. 1397.020
—ununited. 1397.00251. A 19.
—at the neck and trochanters
—united
—comminuted. 1397.005; 1397.012; 1397.022. B; A 15.
—and impacted. 1397.010; 1397.013; 1397.014 (M). B; A 15.
—impacted. 1397.006. A 65.
—oblique. 1397.009. A 15.
—ununited
—gunshot. 1111.828, CCC. A 55.
—at the shaft
—united. 1397.034 (M); 1397.036; 1397.041 (M); 1397.077; 1397.078; 1397.102; 1397.104; 8623 (M); 8631 (M) 8632 (M); 8635 (M). B; A 12; A 15.
—with deformity. 1397.035; 1397.039 (M); 1397.044; 1397.046; 1397.048; 1397.054; 1397.057; 1397.058; 1397.059; 1397.061; 1397.068; 1397.071; 1397.079 (M); 1397.101. B; A 12; A 15.
—comminuted and oblique. 1397.072. B.
—oblique. 1397.0355; 1397.050 (M); 1397.051; 1397.056; 1397.060; 1397.064; 1397.065; 1397.066; 1397.075; 1397.080; 1397.081. B; A 15; A 56.
—with deformity. 1397.030; 1397.032 (M); 1397.033; 1397.038; 1397.040; 1397.047; 1397.052; 1397.070; 1397.093; 1397.096. B; A 15; A 56.
—transverse. 1397.055; with deformity. 1397.049; 1397.073. A 15; A 56.
—gunshot, partially repaired. 1111.818, CCC. A 55.
—ununited. 1397.0625. B.
—comminuted. 1397.082; 1397.084. B; A 15.
— and transverse. 1397.0555. A 15.
—oblique. 1397.037 (M); 1397.074; 1397.089; 1397.092; 1397.094; 1397.095. B; A 15.
—transverse. 1397.062; 1397.076. B; A 15.
—gunshot. 1111.826, CCC; 1397.103; 1397.105. A 12; A 55.
—butterfly. 1111.810, CCC. A 55.
—comminuted. 1111.812, CCC; 1111.816, CCC; 1397.067; 1397.085; 1397.086; 1397.087. A 15; A 55.
—compound, comminuted. 1111.800, CCC. A 55.
—complete. 1111.814, CCC. A 55.
—fissured. 1397.0081. A 54.
—grooved. 1111.822, CCC. A 55.
—oblique. 1111.802, CCC. A 55.
—stellate. 1111.830, CCC. A 55.
—at the shaft and trochanters
—united; oblique. 1397.029; 1397.0395; 1397.045 (M). B; A 15; A 19.
—at the neck, shaft and trochanters
—united; comminuted. 1397.017. A 15.
—ununited. 1397.031. A 15.
—at the condyles
—united. 8629 (M); 1397.011; 1397.099; 1397.100. A 12; A 15.
—comminuted and oblique. 1397.090. A 48.
—intercondyloid. 1397.069 (M). B.
—ununited
—comminuted. 1412.70. A.
—separation of the epiphysis. 1397.091. B.
—gunshot
—with necrosis. 1111.804, CCC. A 55.
—gutter. 1111.824, CCC. A 55.
—intercondyloid. 1111.820, CCC; 1111.808, CCC. A 55.

Patella

—united. 8718 (M). A 62.
—comminuted. 1412.35. B.
—oblique. 1412.05; ligamentous union. 1412.75. B.
—transverse. 1412.10; 1412.15; 1412.30; ligamentous union. 1412.40; 1412.45; 1412.55 (M); 1412.60 (M); 1412.65 (M); 1412.80. B; A 15; A 37.
—stellate. 1412.50 (M). B.
—ununited. 1412.91; 1412.92. A; A 12.
—comminuted. 1412.70. A.
—transverse. 1412.20; 1412.25.
—oblique. 1412.00. A.
—gunshot. 1412.85; 1412.90. A 54.

Tibia

—at the head
—united. 1442.03; 1442.08. A; B.
—comminuted, oblique. 1442.21. A 15.
—ununited; transverse. 1442.13. B.
—gunshot. 1111.920, CCC; 1111.956, CCC. A 55.
—radiating linear. 1111.950, CCC. A 55.
—at the shaft
—united
—with caries and condensing osteitis. 1442.26. A 15.
—with periostitis and ankylosis following fracture. 1442.32. A 15.
—double oblique. 1442.27. A 15.
—oblique. 1442.15 to 1442.20; 1442.24; 1442.25; 1442.31; 1442.34; 1442.36 (M); 1442.37; 1442.39; 1442.40; 1442.41; 1442.55; 1442.60; 1442.65. B; A 15.
—with deformity. 1442.11; 1442.12; 1442.29; 1442.30. B; A 15.
—with periostitis and osteitis. 1442.44. A 15.
—transverse. 1442.33. A 15.
—gunshot. 1442.10; 1442.35. B; A 15.
—with periostitis. 1442.04. A 15.
—comminuted. 1111.918, CCC. A 55.
—ununited. 1442.70; fibula assumed function of tibia resulting in hypertrophy and bowing. 1442.09; 1442.92. B; A 49.
—comminuted. 1442.94. A 12.
—and oblique. 1442.23. B.
—oblique. 1442.75.
—resulting in separation of the epiphysis. 1442.06; 1442.07. B.
—gunshot. 1442.00; 1442.01; 1442.45. A 15; A 54.
—butterfly. 1111.902, CCC. A 55.
—comminuted. 1442.02; 1442.50. A 54.
—complete. 1111.912, CCC. A 55.
—gutter. 1111.930, CCC. A 55.
—transverse. 1111.914, CCC; 1111.916, CCC. A 55.
—at the malleolus
—united; transverse; syphilitic. 1442.42. A 15.
—at the condyles
—ununited; gunshot. 1111.954, CCC. A 55.

Fibula

—at the shaft
—united. 1457.24; 1457.28; with deformity. 1457.12; 1457.20. A 15.
—double oblique. 1457.16. B.
—double involving the ankle-joint. 1427.90. B.
—oblique. 1457.00; 1457.02; 1457.04; 1457.06; 1457.14; 1457.22; 1457.31; 1457.35; 1457.36; 1457.18; 1457.30; 1457.305; 1457.32; with deformity. 1457.08; 1457.10. B; A 12; A 15; A 24.
—ankylosis with the tibia. 1457.29. A 15.
—gunshot. 1457.26. B.
—ununited; gunshot. 1111.926, CCC. A 55.
—at the malleolus
—united; oblique. 1457.33.
—ununited; transverse. 1457.34.

A. 2. Multiple

Vault

—healed; cicatrix after perforating gunshot fracture. 1151.41 (M) (5a).

—ununited. 1151.50. A 12.
—transverse. 1151.37. B.
—gunshot; large square hole and radiating fracture. 1111.126, CCC. A 55.

Vault and base

—healed. 1151.05. A 15.

Vertex and base

—healed. 1151.23 (6a). A 58.

Entire right side of skull

—ununited. 1151.42. A 7.

Skull cap

—ununited; gunshot. 1111.130, CCC; 1111.160, CCC; 1151.44. A 54; A 55.

Bones of the face

—ununited; gunshot. 1111.110. A 55.

Occipital

—and parietal
—ununited. 1151.47; 17830.53. A 12.
—and temporal
—ununited. 1151.21. B.
—gunshot; perforating. 1111.168, CCC. A 55.
—and femur
—ununited; gunshot. 1111.128, CCC. A 55.

Parietal

—and temporal
—ununited. 1151.04; 1151.40; 1151.45. A 12; A 15; A 52.
—and frontal
—ununited; vertical and depressed. 1151.02; 1151.09. B; A 15.
—and temporal
—ununited. 1006.76.
—punctured. 1151.10 (6b). A 46.

Frontal

—and ethmoid
—ununited; depressed. 1151.27. B.
—and nasal and vomer
—ununited; depressed. 1151.29. A 15.
—and temporal, parietal and sphenoid
—ununited; gunshot. 1151.01. A.
—orbit, superior maxilla
—ununited; multiple; gunshot. 1111.140, CCC. A 55.

Temporal

—and sphenoid; ununited. 1151.06. B.
—and zygomatic process
—ununited. 1151.30. B.
—gunshot; radiating. 1111.102, CCC; vertical linear and comminuted. 1111.166, CCC. A 55.
—and frontal and orbital plates
—ununited; gunshot. 1111.105, CCC. A 55.
—and malar bones, superior maxilla, zygomatic arch and orbits
—ununited; gunshot; radiating linear. 1111.100, CCC. A 55.

Superior maxilla, malar bones, nasal bones and orbital plates

—healed. 1169.02. A 15.
—ununited. 1169.01. A 15.
—and fibula
—ununited; gunshot; radiating linear. 1111.104, CCC. A 55.

Malar

—and zygomatic arch
—ununited; gunshot. 1111.164, CCC. A 55.
—and nasal bones
—healed; fissured. 1169.09; 1169.10. B.
—and orbits; ununited; gunshot. 1169.12. A 51.
—and mandible
—united; oblique. 1169.20. B.
—and nasal bones. 1169.03. A 15.

Atlas

—and axis
—ununited; gunshot; comminuted. 1111.200, CCC A 55.
—and orbits
—gunshot. 1111.172, CCC. A 55.

Dorsal and lumbar vertebrae

—partial repair; impacted. 1188.10. A 15.
—ununited; vertical and crescentric. 1188.20. B.

Ribs and vertebrae

—ununited; gunshot. 1111.215, CCC; 1111.216, CCC. A 55.

Arm

—deformity after fracture. 8603 (M).

Humerus

—and metacarpals
—ununited; gunshot 1111.402, CCC. A 55.
—radius and ulna
—gunshot; comminuted. 1277.05. A 54.
—and elbow-joint
—ununited; gunshot; comminuted. 1262.83; 1262.85; 1262.91; 1262.92; 1111.450, CCC; 1111.454, CCC; 1111.452, CCC. A 54; A 55.
—and shoulder-joint
—ununited; gunshot. 1262.89. A 54.

Radius involving the wrist-joint

—at the shaft
—united
—oblique. 1277.65. B.
—comminuted. 1277.45; 1277.86; 1277.50. B; A.
—ununited
—artificial. 1277.78; 1277.80. A 51.
—comminuted. 1277.82; 1277.84. B.
—gunshot
—comminuted. 1277.75. A 61.
—with ankylosis of the wrist-joint. 1277.88. B.

Radius and ulna

—united. 1307.02; 1307.05; 1307.10; 1307.15; 8606 (M); with deformity. 8609 (M). B; A 15; A 63.
—comminuted. 1307.56.
—ununited
—incomplete. 1307.00 (2a). A 62.
—gunshot
—butterfly. 1111.500, CCC. A 55.
—comminuted. 1307.21; 1307.25; 1307.30. A 54.
—fissured. 1307.22. A 54.
—transverse. 1111.502, CCC. A 55.
—and wrist-joint
—ununited; comminuted and compound. 1322.00. A.
—and clavicle, rib and frontal bone
—ununited; gunshot. 1111.301. A 55.

Ulna involving the elbow-joint

—united; oblique; secondary ankylosis of condyles and obliteration of the elbow-joint. 1292.05; 1292.10. B.
—ankylosis of elbow-joint. 1292.00. B.

Carpus and metacarpus

—ununited; gunshot; compound. 1322.20. A 54.
—and phalanges
—ununited
—compound and comminuted. 1322.10. A.
—gunshot; oblique. 1337.10. A 54.
—united. 1336.00; 1337.00. B.

Pelvis and femur

—ununited; gunshot. 1111.712, CCC. A 55.

Innominate bone and sacrum

—ununited. 1367.00; 1382.20. B; A 15.
—gunshot. 1111.710, CCC. A 55.

Ilium

—and sacro-iliac joint
—ununited; gunshot 1111.714, CCC; 1111.700, CCC; 1111.752, CCC; 1111.756, CCC. A 55.
—comminuted. 1111.775, CCC. A 55.
—and femur
—gunshot; comminuted. 1111.716, CCC. A 55.
—and sacral vertebrae
—gunshot. 1111.706, CCC. A 55.
—sacrum and lumbar vertebrae
—ununited; gunshot. 1111.754, CCC. A 55.

Sacrum involving the hip-joint

—ununited; gunshot. 1111.778, CCC. A 55.

Leg

—deformity after fracture. 8720 (M); 8722 (M); 8723 (M).

Femur

—ununited; gunshot; involving the knee-joint. 1111.850, CCC. A 55.
—and tibia
—ununited; gunshot; involving the knee-joint. 1111.852, CCC. A 55.

—and patella
—ununited. 1412.70. A.
—gunshot, involving the knee-joint. 1652.00. A.

Tibia and fibula

—united. 1427.102; 1427.103; 8719 (M); 1427.75; 1427.87. A 12; A 15.
—comminuted. 1427.66. B.
—oblique. 1427.36; 1427.38; 1427.40; 1427.44; 1427.48; 1427.54 to 1427.63 inclusive; 1427.67; 1427.78; 1427.80; 1427.81; 1427.82; 1427.84; 1427.87; 1427.88; 1427.95; 1427.96. B; A 15.
—with deformity. 1427.46 (M); 1427.50; 1427.52; 1427.68; 1427.74; 1427.77. B; A 15.
—compound comminuted. 1427 64; 1442.90. B; A 49.
—intrauterine. 1427.69. A 15.
—Pott's. 1427.75; 1427.85 (M); with deformity. 1427.97. B; A 15.
—transverse. 1427.96; with deformity. 1427.65; 1427.86. B; A 15.
—gunshot. 1111.928, CCC; 1442.22. B; A 55.
—comminuted of fibula; greenstick of tibia. 1111.908, CCC. A 55.
—ununited. 1427.101; 1427.70; 1427.71. B; A 12; A 15.
—comminuted. 1427.14; 1427.24; 1427.99; 1427.100. B; A 12; A 15.
—and transverse. 1427.12; 1427.34. B.
—oblique. 1442.75; 1427.52; union of fibula. 1427.83. A 15.
—compound comminuted. 1427.18; 1427.20; 1427.22; 1427.26; 1427.28; 1427.32. B; A 15.
—double. 1427.30; 1427.34; 1427.84. B; A 15.
—transverse. 1427.42. B.
—and astragalus
—gunshot; comminuted. 1427.06. A 54.
—gunshot
—multiple. 1111.900, CCC. A 55.
—comminuted. 1427.00; 1427.04; 1427.08; 1427.10; 1427.98; 1111.904, CCC, 1111.910, CCC; 1111.922, CCC. A 54; A 55.
—complete. 1111.906, CCC. A 55.
—resulting in separation of the epiphysis. 1427.76; 1427.762. A; A 15.

Tibia and fibula involving the ankle-joint

—united. 1427.90. B.
—comminuted and oblique. 1427.92. A 15.
—oblique. 1427.91. A 15.
—outward dislocation of the ankle-joint. 1427.75. A 15.
—obliteration and ankylosis of the ankle-joint. 1427.93. A 15.
—ankylosis of the ankle-joint. 1427.86; 1427.95. B.
—ununited. 1427.76. A.

Tibia involving the ankle-joint

—ununited; gunshot. 1111.958, CCC. A 55.

Tibia involving the knee-joint

—ununited; gunshot. 1111.854, CCC; 1111.856, CCC; 1111.924, CCC; 1111.952, CCC; 1111.954, CCC; 1111.956, CCC. A 55.

Tarsus

—ununited
—of the neck of the astragalus. 1472.00. B.
—also scaphoid and calcaneum. 1472.05. B.
—comminuted of calcaneum and outer malleolus. 1472.15. A 15.
—united
—of astragalus; transverse; ankylosis. 1472.10. B.

Metatarsus

—united
—with caries and deformity. 1487.00. A.
—oblique. 1487.10. A 15.

Shoulder-joint

—ununited; gunshot. 1262.89. A 54.

Elbow-joint

—united. 1262.98. with deformity. 8605 (M). A 15.
—with ankylosis. 1262.82; 1262.97. B; A 15.
—oblique of ulna. 1292.00; 1292.05; 1292.10. B.

—ununited
—gunshot. 1262.83; 1262.85; 1262.91; 1262.92; 1262.99; 1307.35; 1307.40; 1307.45; 1562.00; 1562.05; 1111.450, CCC; 1111.452, CCC; 1111.454, CCC. A 12; A 54; A 55; A 67.

Wrist-joint

—united with deformity. 8611 (M); 8612 (M); 8613 (M); 8614 (M); 8615 (M); 8616 (M)
—comminuted of the radius. 1277.45; 1277.50; 1277.86. B.
—oblique of radius. 1277.65. B.
—transverse of radius. 1277.70. B.
—gunshot, with ankylosis of the wrist-joint. 1277.88. B.
—ununited
—comminuted of radius. 1277.82; 1277.84. B.
—gunshot. 1277.75. A 61.
—compound comminuted. 1322.00. A.
—oblique of radius. 1277.78; 1277.80. B.

Sacro-iliac joint

—ununited
—gunshot. 1111.714, CCC; 1111.778, CCC. A 55.
—avulsion of, after gunshot. 1111.710, CCC. A 55.
—comminuted. 1111.700, CCC; 1111.752, CCC; 1111.756, CCC; 1111.775, CCC; 1111.778, CCC. A 55.

Knee-joint

—ununited
—gunshot. 1397.097; 1397.098; 1652.00; 1111.850, CCC; 1111.852, CCC; 1111.854, CCC; 1111.856, CCC; 1111.954, CCC. A 54; A 55.
—comminuted. 1652.15.
—linear. 1111.924, CCC. A 55.
—gutter. 1111.952, CCC. A 55.

Ankle-joint

—united
—comminuted, of tibia. 1427.92. A 15.
—double of fibula. 1427.90. B.
—of tibia and fibula. 1427.91; with outward dislocation of the ankle. 1427.75.
—of external malleolus. 1457.33.
—ununited. 1667.00. B.
—crushed. 1427.76. A.
—gunshot. 1111.924, CCC; 1111.958, CCC. A 55.
—comminuted of tibia, fibula and astragalus. 1427.06. A 54.

B. Luxations

Bones articulated with spring wires to demonstrate luxation of bones

—upper extremity. 1125.00.
—lower extremity. 1125.50.

Mandible

—1168.00. A 15.
—subluxation after fracture. 1169.20. B.

Atlas

—1187.00. B.

Humerus

—at the head after fracture of the neck 1262.00. B.
—subcoracoid. 1546.00; 1546.05; 1546.10. B.

Radius and ulna

—with ankylosis. 1561.00. A 15.

Carpus

—1321.00. B.

Metacarpals

—1336.00; 1337.00; 8617 (M). B.

Metacarpophalangeal joint

—with ankylosis. 1336.10. A 15.

Femur

—1636.00; 1636.10; 1636.05 (M); 1636.25; 1636.60. B; A 15.
—with eburnation. 1636.70. B.
—with ankylosis. 1636.35. B.
—with false joint. 1636.50; 1636.60. B.
—on dorsum of ilium. 1636.20; 1636.30; 1636.40. B.

Fibula

—after fracture. 1442.19. A 15.

Astragalus

—1427.75; 1471.00. A; A 15.
—and caries. 1471.05. B.

Knee-joint

—1651.00. B.
—and ankylosis. 1651.10. B.
—and osteitis. 1651.20. B.

C. Diseases

Arthritis

—scapula. 1254.20. A 15.
—humerus. 1262.50. A 15.
—radius. 1284.00; 1284.20. A 15.
—ulna. 1299.00; 1299.20; 1299.40. A 15.
—shoulder-joint. 1262.70; 1269.56; 1554.00; 1554.05; 1554.15. B; A 15.
—elbow-joint. 1269.06; 1269.10; 1269.18; 1269.28; 1269.44; 1269.46; 1269.48; 1269.60; 1269.66; 1269.68. B; A; A 15.
—and wrist-joint. 1314.20. B.
—metacarpal bones. 1344.10. A 15.
—femur. 1404.01; 1404.02; 1404.051; 1404.42; 1404.47. B; A 15.
—tibia. 1449.62. A 15.
—innominate bone and femur (hip-joint). 1644.14; 1644.16; 1644.20; 1644.22; 1644.26; 1644.32; 1644.34; 1644.36; 1644.38 (14a); 1644.40; 1644.43; 1644.44; 1644.46; 1644.50; 1644.52; 1644.56; 1404.05. B; A 15.
—knee-joint. 8707 (M); 8709 (M); 8710 (M); 1397.047; 1397.057; 1435.45; 1449.54; 1659.05; 1659.10; 1659.50 (6f); 6115.00. B; A; A 15; A 63; A 78.
—bones of the foot. 1494.00; 1494.20. B; A 15.
—ankle-joint. 1479 20; 6095.10. A 15.
—and ankylosis
—elbow-joint; traumatic. 1269.80. A 53.
—wrist-joint. 1584.10. A 15.
—femur and pelvis; osteo-arthritis and scissors-like deformity. 1644.60.
—knee-joint. 1659.20; 1659.80 (6c); 1659.45. A 15; A 63.
—and atrophy
—head of humerus; elbow-joint. 1269.42. B.
—head of radius; elbow-joint. 1269.56; 1284.05. B; A 15.
—head and greater trochanter of femur. 1404 02. A 15.
—and caries
—ulna. 1297.10. A 15.
—elbow-joint. 1269.64. A 64.
—femur, tibia and knee-joint. 1657.00. A 63.
—knee-joint. 1659.15. A 15.
—coxitis
—innominate bone; eburnation. 1389.05. A 15.
—with deformity of the acetabulum. 1389.20 (M); 1389.25; 1389.30; 1394.00. B; A 15.
—and femur, with ankylosis. 1644.54.
—and eburnation
—humerus. 1269.04. B.
—shoulder-joint. 1554.10. B.
—elbow-joint. 1269.08; 1269.50. B.
—femur. 1404.07. A 15.
—and innominate bone. 1644.10; 1644.12; 1644.24; 1644.48 (14b). B; A 15.
—knee-joint. 1659.00; 1659.25. B.
—and exostosis
—humerus. 1269.12. A 15.
—ulna. 1299.05. A 15.
—femur. 1404.03; 1404 04. A 15.
—radius. 1284.15.
—innominate bone and femur. 1644.18. A 15.
—and eburnation
—femur. 1404.15; 1404.025; 1404.0251. B; A 15; A 19.
—knee-joint. 1659.55. A 15.
—loose bodies in joints
—knee-joint; cartilaginous. 1664 00; 1664.10.
—and necrosis
—knee-joint of a child of 13 years. 1448.80 (6d). A 63.
—and pressure necrosis
—femur; deformity of the head and arthritis of the hip-joint. 1404.05.

Arthritis and osteitis

—humerus, radius and ulna. 1269.58. A 15.
—innominate bone and femur. 1644.28. A 15.

Arthritis (tubercular)

—femur. 1404.435. A 19.

Arthropathy

—knee-joint. 8701 (M); 8703 (M); 8711 (M).
—and ankle-joint. 8702 (M).

Cancrum Oris

—mandible. 1178.03 (M); 1178.04 (M). A 15.
—and maxilla from a three year old child. 1178.02. A 15.

Osteitis (see also *periostitis* and *arthritis*)

—inferior maxilla. 1179.01. A 15.
—ribs. 1224.14; 1224.16.
—humerus. 1269.20; 1269.26; 1269.22. A 15.
—metacarpals. 1344.00. B.
—femur. 1404.06; 1404.19; 1404.32; 1651.20; 1404.37; 1659.70; 1404.43. B; A 15.
—after fracture. 1396.051. A 15.
—tibia. 1449.38; 1449.40; 1449.60; 1659.75. B; A 15.
—and fibula. 1434.46; 1434.65; 1449.08. B.
—metatarsals. 1494.40. A 15.
—with ankylosis
—humerus and elbow-joint. 1269.02. B.
—and hypertrophy
—humerus, ulna and elbow-joint. 1269.00. A 15
—tibia, fibula and ankle-joint. 1434.50. A 15.
—with caries
—foot. 1477.60. A 15.
—humerus. 1269.24. A 15.
—with exostosis
—ulna. 1299.15. B.
—tibia. 1449.46. A 15.
—and fibula. 1434.40. B.
—with hypertrophy
—sphenoid. 1157.04. A 15.
—humerus. 1269.31; 1269.34; 1269.36. A 15.
—femur. 1404.27; 1404.305. A 15; A 19.
—tibia. 1449.21; 1449.26; 1449.02; 1449.12. B; A 15.
—and fibula. 1434.10; 1434.15. B; A 15.
—fibula. 1464.20; 1464.25; 1464.30; 1464.40. A 15.
—and necrosis of humerus. 1269.38. B.
—medullary abscess of tibia. 1449.28. B.

Osteitis (*condensing*) (see also *fractures*)

—tibia. 1449.22. A 15.
—femur. 1404.40. B.
—with caries of tibia. 1442.26. A 15.
—with hypertrophy
—ulna. 1299.25; 1299.30; 1299.35. A; A 15.
—and caries of the femur. 1404.20. B.

Osteitis deformans (*Paget's Disease*)

—calvarium. 1157.07; 1157.09 (M). A 69; A 70.
—with hyperostasis. 1157.06 (7a; 8a). A 68.

Osteitis (*rarefying*)

—fibula. 1464.05; 1464.10. A 15.
—and hypertrophy of tibia. 1449.04.

Osteitis (*syphilitic*)

—calvarium. 1161.08. B.
—tibia. 1449.14; 1449.34; 1449.44; 1449.50; 1449.18. B; A 15.
—with ankylosis of tibia and fibula. 1434.35. B.
—with hypertrophy
—humerus and ulna; probably syphilitic. 1269.47. A.
—radius and ulna; probably syphilitic. 1314.10.
—tibia. 1449.24; 1449.45; 1449.52; 1449.10; 1449.16; 1449.20; 1449.12. B; A 15.
—fibula. 1467.10. B.

Osteomalacia

—pelvis. 1365.21 (M); 1365.25 (M); 1365.34 (M) (9a); 1365.41 (M). A 11.
—pseudo-osteomalacia
—pelvis. 1365.18 (M) (9b); 17834.40. A 11.

Osteomyelitis

—femur. 1404.31. A 69.
—tibia and fibula. 1434 55. A 15.
—skull; arrested case. 1153.00.
—with exostosis of femur. 1404.38. A 15.

Periostitis

—humerus. 1269.30. A 15.
—femur. 1404.21; 1404.35. A 18. B.
—with ankylosis of tibia and fibula following fracture; probably syphilitic. 1442 32. A 15.
—with caries
—tibia. 1447.20; 1657.20. B; A 51.

—femur. 1402.00. A 15.
—humerus, radius and ulna. 1269.52. A
—and hypertrophy of tibia. 1449.00.
—with exostosis
—femur. 1404.23. A 15.
—tibia. 1449.32; 1449.48. A 15.
—and fibula. 1434.60.
—and hypertrophy of fibula. 1464.00; 1464.15; 1457.12. B; A15.
—with necrosis
—tibia. 1448.10; 1448.55. A 15; A 19.
—and hypertrophy of tibia and fibula. 1433.00. B.
—and pressure necrosis of head of humerus. 1553.00. B.

Periostitis and condensing osteitis

—tibia. 1449.06. A 15.
—with hypertrophy of femur. 1404.28; 1404.34. B; A 15.

Periostitis and osteitis

—humerus. 1269.40. A 15.
—femur. 1404.25. A 15.
—with exostosis of tibia and fibula. 1442.44. A 15.
—with necrosis of humerus. 1269.32. A 15.
—with cavity and deformity of femur. 1404.33.
—with hypertrophy of femur. 1404.30. B.

Periostitis (syphilitic)

—tibia and fibula. 1434.48; probably syphilitic. 1442.32. B; A 15.
—femur. 1407.00; probably syphilitic. 1404.26. B; A 15.

Rickets

—skeleton of a rachitic woman upon whom Cesarean section was performed. 1145.75 (10a; 11a). A 75.
—pelvis. 1365.02 (M); 1365.03 (M); 1365.04 (M) (9c); 1365.16 (M); 1365.17 (M); 1365.19 (M); 1365.24 (M); 1365.36 (M) (9d); 1365.40 (M) (9e); 17834.43. A 11; A 83.
—femur
—and periostitis. 1405.05. A 15.
—with anterior curvature. 1405.50; 1405.55; 1405.551; 1405.40; 1405.30; 1405.20; 8716 (M). B; A 15; A 19.
—with anteroposterior curvature. 1405.00. B.
—tibia
—with anterior bowing. 1435.20. A 15.
—with anteroposterior bowing. 1435.30; 1435.40. A 15.
—and fibula
—with internal bowing. 1434.00. A 15.
—with anterolateral bowing. 1435.10. A 15.
—skull of a juvenile with relatively large anterior fontanelle. 17830.54.

Syphilis (see also *periostitis*, *osteitis*, *caries* and *necrosis*)

—clavicle. 1242.00.
—tibia. 1442.42. A 15.

Tuberculosis

—vertebrae. (Pott's Disease). Anteroposterior curvature. 1194.00; 1194.05; 1194.20; 1194.30; 1194.40; 1194.50; 17830.72. A; A 58; A 15.
—primary, of spinal arches. 1194.16.
—and ribs. 1194.10; 1194.15. A; B.
—part of vertebral column, ribs and pelvis showing cold abscess injected. 1194.06.
—femur. 1404.12. B.
—hip-joint (coxalgia). 1408.15.
—and ankylosis
—vertebrae. 1194.55; 1194.25; 1194.35. A 15.
—hip-joint (coxalgia). 1644.00. A 15.

Tumors

—odontoma. 1023.383, C-140. A 14.
—osteosarcoma
—humerus. 1273.00. A 15.
—wrist. 6310.25; 6310.26; 6310.27. A 15.
—jaw. 6520. A 15.
—epulis. 6310.42; 6310.43; 6310.432. A 15.
—innominate bone. 1393.05. A 15.
—buttock. 6310.30. A 15
—femur. 6310.47; 6400.06; 8805 (M). A 7; A 15.
—tibia. 6310.40; 1453.50; 1453.51 (12a); 8804 (M); 6310.48. A; A15; A 76.
—and fibula. 6310.41. A 15.
—region of the knee. 6480.30.
—knee-joint. 6310.44. A 24.
—section of. 6310.445; 6310.45. A 15.

—round-cell sarcoma
—temporal bone. 6310.10. A.
—sarcoma
—clavicle. 6310.00. A 63.
—jaw. Designated as "sarcoma." 1172.-50 (13 a)
—scirrhus cancer of the humerus. 6470.13.
—unspecified
—mandible. 1182.15. A 15.
—antrum. 8764 (M).
—scalp, in intimate contact with skull. 6400.00. A 15.
—femur. 8757 (M).

D. Pathological Changes in Bone

Abscess

—cavity in hard palate. 1006.052. B 4.
—from second molar opening through the floor of the right maxillary sinus. 1023.338; 1023.-400, C-225. A 14.
—within maxillary sinus and infra-orbital sinus. 1023.340, C-223–224. A 14.
—near root of first molar. 1023.404, C-221–222. A 14.
—perforating floor of nose. 1023.405. A 14.

Ankylosis (see also *fractures, Pott's Disease, arthritis, tuberculosis, periostitis, osteitis, caries, exostosis* and *luxation of bones*)

—jaw. 1008.50; C-358-359; 1023.302, C-356-357. A 15.
—bones of the vertebrae column. 1183.20; 1183.30; 1194.75; 1194.77; 1194.78; 1194.79; 1194.80; 1194.834; 1194.835; 1194.840; 1194.-848; 1194.850; 1194.868; 1194.870; 1194.915; 1194.925. A; B; A 15; A 16.
—in female skeleton; curvature. 1145.60. B.
—and ribs. 1194.842. A 15.
—and sacrum 1194.900. A 15.
—rib and manubrium. 1224.05; 1224.10. A 15.
—radius and ulna. 1314.00; 1314.15. A; A 15.
—shoulder-joint. 1554.20. B.
—elbow-joint. 1561.00; 1569.00; 1569.05; 1569.10; 1269.70; 1269.72, 1269.74; 1269.78; 1299.45. A B; A 12; A 15.
—wrist-joint. 1584.00; 1584.35; 1584.20; 1584.-30. A; B; A 15.
—first phalanx. 1336.10. A 15.
—tibia and fibula 1434.25; 1434.45; 1434.47. A 15.
—knee-joint. 1454.00; 1659.35; 1659.40; 1659.-60. B; A; A 15.
—ankle-joint. 1479.00. B.
—tarsometatarsus. 1494.30. A 15.
—hip-joint. 1644.30; 1644.58. A 7; A 15.
—sacro-iliac joint. 1629.00. A 15.
—and atrophy
—vertebrae. 1194.836. A 15.
—tarsometatarsus. 1479.40; 1489.00; 1689.00. A 15.
—and caries
—vertebrae. 1194.872; 1194.846; in skeleton, with spinal curvature. 1145.65. B; A 15.
—femur, tibia and patella. 1651.30 A 15.
—foot. 1659.65. A.
—and exostosis
—vertebrae. 1194.838; 1194.844; 1194.-920; 1194.930; 1194.950. B; A 15.
—ankle-joint. 1479.10. A 15.

Atrophy (see also *ankylosis* and *arthritis*)

—after fracture
—nasal bones. 1169.03. A 15.
—head of humerus. 1262.20. B
—head of radius. 1277.15. B.
—tibia. 1442.09. B.
—maxillary bone. 1008.76. A 14.
—vertebrae. 1191.00; 1191.10. A 15
—phalanges. 1350 00. A.
—heel. 1474.00. B.

Caries (see also *periostitis, osteitis, arthritis* and *exostosis*)

—skull. 1155.05; 1155.06. A 1
—sphenoid bone. 1155.00; 1155.01. A 15.
—calvarium. 1155.04; 1155.09. A 7; A 12.
—frontal bone. 1169 07. A 15.
—temporal bone. 1155.02. A 16.
—ear. 1059.010; 1100.244; 1100.262. B 4; A 45.
—antrum. 1176.01. B.
—maxilla. 1176.00. B.
—mandible. 1176 02. B.
—vertebrae. 1194.60; 1194.65; 1194.70; 1194.-76; 1194.47. A 15; B; A 19.
—and sacrum of a child. 1194.910. B.
—sternum. 1207.00; 1207.10. A 15.

—clavicle. 1237.00; 1237.05; 1237.10; 1237.15; 1237 20. B; A 15; A 16.
—after fracture. 1232.16.
—causing fracture. 1237.25. A 15.
—scapula. 1254.30.
—radius. 1282.10. A 15.
—ulna. 1297.15. A 15.
—phalanges. 1357.00. B.
—thumb. 6155.00. A 15.
—innominate bone. 1287.10. A 16.
—sacrum. 1372.00; 1372.05; 1194.905. B; A 1; A 15.
—femur. 1642.00; 1402.05; 1402.10; 1402.15; 1402.20; 1402.25; 1402.30; 1402.35. A 1; A 15.
—after fracture. 1397.082. B.
—tibia. 1447.05; 1447.10; 1449.42; from a child. 1447.25. A 1; A 15; A 51.
—fibula. 1462.00. A 15.
—bones of the foot. 1492.05; 1477.40; 1447.50; 1477.35; 1471.05; 1477.70; 1477.80; 1487.00; 1477.00; 1477.20; probably tuberculosis. 1672.00. A; A 15; A 19.
—shoulder-joint. 1552.00. A 19.
—knee-joint. 1657.40; 1659.81. A 19; A 49.
—probably tuberculosis. 1657.10; 1657.30. A 19; A 63.
—hip-joint. 1462.05.
—and ankylosis of
—vertebrae. 1145.55; 1194.866. B; A 15
—elbow-joint. 1269 84. A 15.
—and necrosis of
—humerus, ulna, radius and carpus. 1283.-30. A 17.
—and exostosis of
—radius. 1282.05. A 15.
—femur. 1404.45.

Caries (*syphilitic*)

—skull. 1161.10; 1161.11; 1161.12; 1161.03; 1161.02; 1161.01; 1161 00. B; A 1; A 15; A 42.
—calvarium 1161.05; 1161.06. A 15.
—ulna; probably syphilitic. 1302.00. B.

Cysts

—maxillary dental. 1008.45. A 14.
—dentigerous, of right mandible. 1023.435. A 14.

Eburnation (see also *arthritis*, *exostosis* and *fractures*)

—mandible. 1172.11. A 7.
—innominate bone; rim acetabulum worn and eburnated as though by subluxation of femoral head. 1394.05. A 15.

Exostosis (see also *periostitis*, *osteitis*, *arthritis*, *caries* and *osteomyelitis*)

—skeleton. 1145.50.
—skull
—calvarium; inner table. 1157.00. A 15.
—parietal bone; inner table. 1157.02; 1157.03. A 8.
—temporal bone; external auditory canal. 1157.05. A 15.
—maxilla. 1166.00; 1023.342, C-227–228. A 14.
—roof of maxillary sinus. 1023.409, C-178–179. A 14.
—in membrane of maxillary sinus. 1023.-419, C-206. A 14.
—alveolar process. 1179.00. A 15.
—vertebrae. 1194.81; 1194.82; 1194.832; 1194.-854; 1194 856; 1194.858; 1194.860; 1194.862; 1194.864; 1194.874; 1194.876; 1194.955. A 15.
—ribs after fracture. 1217.02; 1217.38. B; A 15.
—clavicle. 1239.00; 1239.10; 1239.20; 1239.30. A 15.
—and scapula. 1554.02. A 15
—scapula. 1254.10. B.
—humerus. 1262.80; 1269.16; 1269.17. A 1; A 15.
—radius. 1284.10. A 15.
—back of hand. 6400.05; 8754 (M). A 15.
—pelvis. 17834.37 (M); 1374.10. B; A 11.
—innominate bone. 1389.00; 1389.10; 1389.15. A 15.
—after fracture. 1382.50. B.
—and femur. 1644.42. A 15.
—femur. 1404.17; 1404.18; 1404.24; 1404.245; 1404.29; 1404.295; 1404.296; 1404.36; 1404.39; 1404.41; 1404.46; 1404.49; 1404.44; 1404.50; 1401.00; 1397.0625. B, A 1; A 15; A 24.
—after fracture. 1397.00251; 1397.026. A 15; A 19.
—tibia. 1449.56. A 15.
—and fibula. 1434.00; 1434.05; 1434.20; 1434.30. B; A 15.
—fibula. 1464.35. B.
—metatarsal. 1494.60. A 15.
—big toe (ungual). 6004.00; 6004.5. A 67.
—and ankylosis
—pelvis; sacro-iliac joint. 1374.00; 1374 - 10. B.

—and caries.
—radius. 1282.05. A 15.
—femur. 1404.45.
—and eburnation of femur. 1404.10 (14c). A 71.
—and fenestration of scapula. 1254.00. A.
—and necrosis
—clavicle. 1232.26. B.
—femur. 1403.20. B.

Hyperostosis (see also *periostitis* and *osteitis*)

—calvarium. 1152.00. B.
—palate; skull of a male, age 23 years. 1006.85. B 4.
—ribs with lateral curvature of the spine. 1192.40. A 15.
—fibula. 1442.09. B.
—radius. 1284.25. B.
—and caries
—radius. 1282.00. A 15.
—tibia. 1449.36. A 15.
—and exostosis of calvarium. 1157.01. A 15.
—and necrosis of radius. 1283.00. A 15.
—and osteoporosis
—vertebral column, scapula, clavicle, humeri, radii, ulnae, phalanges, ilium, femur, tibia, fibula and patella. 1126.17 to 1126.31 inclusive (15a). A 68.

Necrosis (see also *periostitis*, *osteitis*, *arthritis*, *caries* and *exostosis*)

—skull
—frontal, sphenoid and maxillary bones. 1156.00. B.
—frontal, left malar and maxilla of a child. 1177.01. A 15.
—temporal bone; roof of tympanum and mastoid antrum; otitis media. 1156.10. 1156.20 (2b). A 72.
—of external auditory canal. 1157.04 (A); 1157.04 (B).
—face. 1177.00. A 15.
—superior maxilla. 1177.14; 1023.399, C-185–186–187–188. A 15.
—mandible. 1177.03; 1177.035; 1177.025; 1177.02. B; A 15; A 37.
—phosphorus necrosis. 1177.04; 1177.05; 1177.06; 1177.08; 1177.09; 1177.10; 1177.11. A 74.
—after fracture. 1177.07. A 74.
—after variola. 1177.13. A 74.
—internal wall of the orbit. 1023.442, C-189–190–191–192–193. A 14.
—vertebrae. 1195.05. A 15.
—ribs; probably tuberculosis. 1192.05. A 12.
—clavicle. 1238.00; 1238.05. B; A 15.
—scapula. 1253.00. B.
—humerus. 1268.00; 6175.05. A 15.
—with separation of the epiphysis. 1262.25. B.
—and secondary fracture. 1268.10 (6e). A 7.
—and radius. 1269.85. A 19.
—radius. 1283.20; 1283.30. B; A 17.
—central necrosis. 1283.10. B.
—femur. 1403.00; 1403.10. B; A 51.
—after amputation. 6175.02. A 15.
—after fracture. 1397.0355; 1397.074; 1397.076; 1397.091. B; A 15; A 51.
—tibia. 1433.05; 1448.40; 1448.50; 1448.70; 1448.20. B; A 15.
—and astraglaus. 1448.60. A 15.
—diaphysis and epiphysis. 1448.00. A 63.
—fibula. 1463.00. A.
—ankle-joint. 1658.00. B.
—sequestra. 6170.15; 6170.00. A 15.
—from maxilla; tubercular necrosis. 1023.387, C-46. A 14.
—from mandible. 1023.395, C-52.
—produced by the use of hydrogen peroxide. 1023.418, C-39. A 14.
—and ankylosis and exostosis of vertebrae. 1194.45. B.

Necrosis (*syphilitic*)

—skull
—frontal and malar bones, mandible, vomer and alveolar process. 1161.07. B.
—frontal and parietal bones. 1161.04. A 15.
—parietal bones. 1161.09. B.
—face. 1181.05; 1181.00. A 15.

Osteosclerosis

—mandible. 1023.412, C-45. A 14.

Pressure necrosis

—maxilla. 1023.406, C-181–182. A 14.
—sternum. 1128.00. A 27.
—from aneurism of the arch of the aorta. 2082.06. A 15.

—manubrium; aneurism of the arch of the aorta. 1206.00. A 27.
—sacrum, after fracture. 1188.45. A 15.
—humerus
—after fracture. 1262.26. A 19.
—with eburnation and atrophy. 1266.10; 1266.00. B.
—femur. 1401.05 (14d). B.
—after fracture. 1397.004. B.
—with caries. 1397.082. B.
—with exostosis. 1401.00. B.

Rarefaction

—first metatarsal. 1494.50. A 15.

TRANSACTIONS & STUDIES

of the

College of Physicians of Philadelphia

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President's Address*

By J. PARSONS SCHAEFFER

ANOTHER academic year of the College of Physicians of Philadelphia is about to come to a close, the concluding business of the year being the delivery of an annual address by the President of the College. Not only is this a custom of long standing but the Ordinances and By-Laws make it mandatory that the annual address shall be delivered at the Stated Business Meeting of the College, in January. We are now assembled in such meeting and as your President I consider it a privilege to bring you information concerning the general state of the College and to review briefly the varied activities of the College during the past year in the furtherance of scientific medicine and worthy public relations.

The total Fellowship of the College (as of December 31, 1947) numbers 787, of which 725 are Resident Fellows; 51, Non-Resident Fellows; six American Honorary Fellows; three Foreign Honorary Fellows; and two, Honorary Associate Fellows. Special College Privileges have been granted to a group of 15 investigators.

The Sections of the College are constituted as follows: Ophthalmology, 58 active members; Otolaryngology, 57 active members and four honorary members; General Medicine, 148 active members; Public Health, Preventive and Industrial Medicine, 28 active members; Medical History, no report. (The activities of this Section were suspended during the period of the war but will again be resumed in the near future.)

During the calendar year 1947, 57 new names were added to the roll of Resident Fellows; one, to the roll of Non-Resident Fellows; and three, to the roll of Honorary Fellows. The considerable increase in the number of Resident Fellows during the past year is largely due to the return of a group of eligible physicians within a relatively brief period of time from the several War Services.

The College of Physicians has suffered great loss through death during the past year of ten Resident Fellows and one Non-Resident Fellow. As individuals, all of these Fellows were interested in the welfare of the College and some gave outstanding service to the College in varied positions of trust and honor over a goodly number of years. Then, too, among them are those who were widely known for the part they played in advancing the interests of special branches of medicine and surgery. Others gave of their talents and time over a relatively long period of years in promoting the standards of medical education and the cause of organized medicine.

All of the deceased were worthy Fellows of the College and I feel saddened in recording the

* Delivered at the business meeting of the College, 7 January 1948.

names of those who recently sat with us, discussed medical problems with us, and met with us at social gatherings, but now have joined the immortal caravan whence no traveller returns. In honor of the memory of these Fellows, I would ask the living Fellows of the College, here and now assembled, to stand during the reading of the names of our departed friends and colleagues.†

Resident Fellows

David J. Boon
Samuel Bradbury
Warren B. Davis
Irving W. Hollingshead
Walter I. Lillie
George P. Muller
P. S. Pelouze
William Pepper
William T. Sharpless
Richard Manges Smith

Non-Resident Fellow

John H. Musser, Jr.

It is gratifying to report that the College was enabled to meet its budget commitments and appropriations recommended by the Finance Committee, voted by Council in December 1946, and approved by the Fellows at the annual Business Meeting of the College in January 1947. These appropriations provided for the many usual and required activities of the College for the year just ended. In addition, the appropriations made it possible to care for certain replacements and repairs in and about the College Hall, as listed below:

The entire exterior of the building was painted, a repair much needed; certain hot and cold water lines were renewed; a new remote control switch was installed in Cadwalader Hall; the ceiling of the Mütter Museum was repaired and painted; a considerable number of chairs were newly upholstered and refinished for the Reading Room, Dining Room, and Periodicals Room; a new gas hot water heater was installed; and certain rugs were cleaned and repaired.

† For dates of election and death, see necrological list, p. 190.

A replacement not anticipated in the appropriation made to the Hall Committee at the beginning of the year was the complete rebuilding of the skylight of the College Hall. This became an emergency matter during the past summer when it was disclosed that the metal work, general supports and the glass had greatly deteriorated, and the skylight as a whole had become a hazard to those using the building. I am glad to say that a new skylight is now in place and that the lighting of the stairway and its surroundings is greatly improved. (It will be recalled that the skylight in question lights the main approach to the marble stairway leading to the Library, Reading and Periodicals Rooms, and Mitchell Hall, all located on the second floor. The skylight was originally built and assembled at the time of the erection of the present College Building, in 1908.)

Thanks are due the Hall Committee and the Superintendent of the College Hall for their constant attention and interest in the physical plant of the College.

In his annual report last year your President advanced the cause of the Library and referred to the urgent and immediate need of additional funds to enable the College to aid more adequately its Library. The accumulation of foreign journals, due to the war, the increased cost of domestic and foreign journals, books and periodicals, and the heavy charges for binding had brought new financial difficulties. At the time it was suggested that voluntary contributions by the Fellows, or, perhaps, a moderate increase in the annual contribution might solve the problem. The voluntary-contribution method was tried and this proved moderately successful. Because of this success, I wish to commend the Fellows of the College who made voluntary contributions in addition to the regular annual contributions in support of the Library at a time when additional funds were sorely needed. Then, too, I am pleased to report that the American Philosophical Society made a contribution of $3000 from its research funds to aid our Library, this in recognition of the great importance of the Library of the

College of Physicians of Philadelphia in advancing the cause of research in medicine and science generally.

This grant from the American Philosophical Society came to us largely because the College of Physicians, through its Fellows, was giving positive evidence of helping itself. Thus the voluntary contributions by the Fellows of the College and, in essence, the duplication of this effort by the American Philosophical Society made possible the completion of the files and the binding of many of the foreign medical and scientific journals that had accumulated during the last war period. Again the College is grateful to its participating Fellows for their spirit and support. Thanks are expressed to the American Philosophical Society for its generosity and recognition of our Library as a center furthering research.

I venture the belief that every Fellow wishes to see continued growth in influence and usefulness of the College of Physicians. Among the more important assets of the College, the Library, I believe, stands foremost. In view of this, I bespeak the continued interest of every Fellow with reference to voluntary contributions to be applied together with other available funds to the maintenance and further growth of our Library.

The Library Committee of the College was very active during the past year. It wrestled with many knotty problems and on occasions referred important matters to Council of the College for decision. Some of the Committee's activities led to the recommendation by Council that the By-Laws of the College be changed so as to enable Council to make more advantageous use of its present power with reference to contributions from Non-Fellows for the privilege of taking books out of the Library. This matter was recently referred to the Fellows of the College for vote and the Secretary has just reported that the amendment was approved by an overwhelming majority.

The Librarian, Mr. McDaniel, to whom we are indebted not only for his interest and ability in directing the Library but for participation in sundry ways in advancing the cause of the College, has again prepared a lengthy annual report bearing on the general conditions of the Library and its operation. His report merits careful reading.

In order to place the Finance Committee of the College in a better position to consider and make adjustments in the portfolio of the College to meet changing economic and financial conditions as they arise from time to time, counsel for the College reviewed the instruments governing all gifts and bequests made to the College of Physicians and gave an opinion as to the eligibility of the various trust funds for inclusion in one or other of two common trust funds.

Thus, during the past year pursuant to authority granted by the Council of the College of Physicians on recommendation by the Finance Committee and under supervision of Mr. Eric A. McCouch, counsel for the College, virtually all of the trust funds held by the College of Physicians were placed in one of two common trust funds: (1) A Discretionary Common Trust Fund in which funds over which the College of Physicians has broad investment powers might be invested in bonds and shares of preferred and common stock; and (2) A Legal Common Trust Fund in which funds of certain restricted trusts might be invested in securities eligible for trust investments under Pennsylvania Law. A new system of bookkeeping by the College of Physicians relative to its trust funds was installed by Main & Company, Certified Public Accountants. With the cooperation of The Pennsylvania Company, acting as agent for the College of Physicians and as custodian for its securities, the two common trust funds were placed in operation. It is anticipated that this change will result in greater safety for the invested funds of the College as well as simplifying their administration.

Certain funds of the College, relatively few in number, were not considered eligible either for the Discretionary Common Trust Fund or the Legal Common Trust Fund but must in each case be kept separate and apart as a single fund.

Upon the recommendation of the Finance Committee of the College, the fiscal year of the College was changed by the Council of the College to end November 10 of each year. It was decided that there should be an annual audit and review of the books of the College by Main & Company, Certified Public Accountants. It is the opinion of our counsel, Mr. McCouch, that these changes will greatly assist the treasurer in preparing his annual report and will serve to keep the bookkeeping methods of the College of Physicians on an efficient basis.

In concluding this part of my report I wish to express great appreciation to Council of the College; the Finance Committee of the College; Mr. Eric A. McCouch, counsel of the College; and Main & Company for their interest and attention in effecting the changes in our financial structure indicated herewith. The administration is indebted to Miss Olga Lang, clerk of the College, for her faithful and efficient clerical service in connection with the financial program of the College.

From January to May 1947, The College of Physicians and the Philadelphia County Medical Society continued in uniting their efforts in the interest of scientific programs, stated meetings being held alternately in the College and the County Society Halls during this period. This brought to an end the joint-program plan in operation during the period of the war and continued for some time afterward. The governing bodies of the College of Physicians and the County Medical Society were fully appreciative of the helpful and coordinating spirit that came into being because of this joint effort over a number of years and rather reluctantly decided to recommend that the two organizations should again return to the state of individual programs. It was felt that if too much time is consumed in a common effort that the real functions and opportunities peculiar to each organization will fail of the greatest accomplishment possible.

In view of this thought, the College of Physicians and the County Medical Society decided to return to individual programs save that two joint scientific meetings shall be held yearly, one in the Hall of the College of Physicians and the other in the Hall of the County Medical Society. Thus, beginning with the scientific program of the College in October 1947 there was a return to an individual program as in the pre-war years, save as mentioned above with reference to two joint scientific meetings. Despite this, it is believed that the friendly and helpful relationship now existing between the two organizations will continue.

At the beginning of the academic year a new By-Law became operative, giving to the President of the College greater freedom in the selection of the members of the Committee on Scientific Business. The new By-Law permits the inclusion of members of two Standing Committees and the four Prize and Lectureship Committees and any other eligible Fellows whose inclusion might facilitate the work of this important Committee. Thus, the chairman of each committee brings to the Committee on Scientific Business information and decisions from an allied committee. The experience during the past year indicates that this change makes for an effective Committee on Scientific Business.

The Mütter Museum is becoming more and more established as a center of scientific interest. The large list of visitors during the past year is indicative of this. During the year the Mütter Committee and Mrs. Wade, the curator, began an index of all the specimens and objects found in the Museum. Although this index has not been completed as yet, much progress has been made. The Committee has been very active during the year and its annual report will be published in the *Transactions & Studies* of the College. As curator, Mrs. Wade, has shown herself courteous, attentive and capable.

The Committee on Public Health, Preventive Medicine and Public Relations was active in behalf of the College, also variously coordinated its efforts with other similar bodies in effecting better public relations and improving public health conditions in Philadelphia and its environs. Certain members of the Committee were active also in opposing the enact-

ment into law of obnoxious bills introduced during the last session of the State Legislature.

The Committee on Entertainments, Dr. Gilson C. Engel, Chairman, again performed its duties in a praiseworthy manner.

The Alvarenga Prize of the College of Physicians was awarded to Joseph D. Aronson, M.D., United States Bureau of Indian Affairs, on July 14, 1947, in recognition of his outstanding services, studies and observations in the control of tuberculosis in connection with the Bureau of Indian Affairs. On the evening of November 5, Dr. Aronson delivered the Alvarenga Prize Lecture VII to a large and attentive audience in Mitchell Hall of the College on the subject, "The Evaluation of BCG Vaccine in the Control of Tuberculosis."[1]

The College of Physicians was a co-exhibitor with the American Medical Association of items of historic interest and value on the occasion of the Centennial Celebration of the American Medical Association at Atlantic City, June 1947. The item of this exhibit which attracted wide attention was the original and now historic Registration Book of Delegates to the National Medical Convention, of May 1847. This convention was held in Philadelphia and it led directly to the founding of the American Medical Association. The Registration Book, the property of the Library of the College of Physicians, contains the original signatures of the 233 Delegates in attendance at the Convention. Of the 233 Delegates who signed the Registration Book of Delegates to the National Medical Convention of 1847, 15 represented the College of Physicians of Philadelphia.

For attention given this exhibit, the College is grateful to Mrs. Ella N. Wade, curator and custodian, and to Dr. Leandro M. Tocantins, member of the Committee on Mütter Museum.

The *Transactions & Studies* of the College of Physicians of Philadelphia again appeared quarterly under the direction of the Committee on Publication and W. B. McDaniel, 2d, editor. During the year an effort was made by some groups to enlist the College's participation in a plan to establish a new journal devoted to the scientific work of Philadelphia physicians and research workers. Although some desirable points were advanced in favor of the plan, there appeared many objectionable features and some unsurmountable difficulties. The Publication Committee of the College recommended that the *Transactions & Studies* be continued as an independent journal. This recommendation was approved by Council of the College and the *Transactions & Studies* continues to be published under absolute authority of the College of Physicians without any entangling alliances. The publication will continue to bring to the attention of its readers information bearing on the varied activities of the College. Important also is the fact that, apart from the College's open scientific meetings, the *Transactions & Studies* is the medium through which the College of Physicians makes contacts with other libraries and medical and other scientific groups, and through exchanges brings to our Library many other publications.

Attention is directed to the reports of the Officers and Committees of the College and to the Officers of the Sections of the College. Some of these reports will be published in the *Transactions & Studies* of the College; all are now available to the Fellows for reading in the Office of the College.

Although one always wishes for greater activities and achievements, I feel justified none the less to report that the College of Physicians of Philadelphia has had another successful year in carrying forward its program in the interests of progressive and scientific medicine, in meeting the urgent needs of the Library and of the Hall of the College, in effecting better public relations, in voicing its opinion with reference to the enactment of adequate and proper health laws, and in the promotion of good fellowship and coordination in the medical field in Philadelphia and its metropolitan area.

For this success, your President feels greatly indebted to the Officers of the College, Members of Council, the Elective and Standing Committees, the Prize and Lectureship Com-

[1] To be printed in the April, 1948, issue of the *Transactions & Studies*.

mittees, the Trustees of Special Funds, the entire Fellowship, and all employees occupying important places, for their constant interest and effort in behalf of the College.

With the conclusion of this Business Meeting, the College of Physicians of Philadelphia enters upon a new academic year. And, while it is impossible to foresee the many and varied problems that may confront us in the immediate future, we may go forward, I believe, in full anticipation of erecting another milestone of splendid achievement a year hence and thus continue the distinguished record of this historic College.

Memoir of George P. Muller

By THOMAS A. SHALLOW

WITH the death of Dr. George P. Muller on February 18, 1947, the medical profession lost the services of an outstanding figure in American Surgery. The forty-eight years of his professional life were progressive steps in accomplishment.

Dr. Muller was born in Philadelphia on June 29, 1877, the son of Philip R. and Frances (Hughes) Muller. His preliminary education was obtained in the grade schools of Philadelphia, following which, he graduated from Central High School in the year 1895. Here, George Muller showed the first evidence of leadership. He was a good student and although he took no active part in athletics, he was one of the prominent figures in all of the School's social and academic activities.

His medical education was obtained at the University of Pennsylvania, and following his graduation from that institution in 1899, he interned in the Old German Hospital (Lankenau). While serving in this capacity the admiration which he manifested for the late Dr. John B. Deaver's surgical skill, diagnostic ability and originality, gradually developed into a strong friendship which, in no small way moulded his future life. No one who knew Dr. Deaver could help being vastly benefited and improved by his dynamic personality and his ability.

At the completion of his internship, Dr. Muller began as a Junior teacher in the Department of Anatomy of the University of Pennsylvania, under the guidance of the late Dr. George A. Piersol, and out of this long association, a warm and lasting friendship developed. On the death of Dr. Gwilym G. Davis, Dr. Muller was selected to revise Davis's "Applied Anatomy"—which was and is the standard text-book on this subject.

Dr. Muller began his surgical training under the late Dr. Charles H. Frazier as a junior assistant. His rapid rise through the various ranks resulted in his election to the Professorship of Clinical Surgery in 1933, a position which he filled with honor and distinction. He surrendered it to become the Grace Revere Osler Professor of Surgery at Jefferson Medical College, succeeding the late Dr. Edward J. Klopp, and serving in this capacity from 1936 to 1946 when he resigned because of ill health.

Dr. Muller not only served as an undergraduate teacher at the University of Pennsylvania and at Jefferson, but he also held the Chair of Surgery at the Graduate School of Medicine of the University of Pennsylvania from 1918 to 1933 and for several years he was Chairman of the Postgraduate Clinics of Philadelphia. Following the death of Dr. Deaver, Dr. Muller returned to Lankenau Hospital to become one of its surgeons. In addition, he was surgeon to Misericordia Hospital, The Children's Hospital, and the Mary J. Drexel Home, as well as being a consulting surgeon to numerous suburban institutions.

Because of his many hospital associations, Dr. Muller had the opportunity to train young men to carry on the art and the traditions of surgery. The names of men who benefited by this association are too numerous to mention.

Dr. Muller served his Country in both World Wars. He was actively engaged in the Inspector General's Department with the rank of Major in the first World War, and was a consultant to the Surgeon General's Office in the second World War.

He contributed prolifically to medical literature and was a contributor to a number of text-books on surgery. He was a member of the Editorial Board of the *Annals of Surgery*. He received honorary degrees from both Villanova and Muhlenberg Colleges.

Few men have the honor of being recognized as a leader in so many fields of Medicine. Dr. Muller served as President of the College of Physicians of Philadelphia, the Philadelphia Academy of Surgery, the Philadelphia County Medical Society, the American College of Surgeons and the American Association for Thoracic Surgery. He was also a member of the American Surgical Association, the American Medical Association, the Medical Society of the State of Pennsylvania and the Jefferson Society for Clinical Investigation.

Dr. Muller's accomplishments will live long in the memory of those who knew him and his achievements will be an inspiration to coming generations.

Memoir of Warren B. Davis*

By AUSTIN T. SMITH

WARREN B. DAVIS, son of Luther A. and Mary Donnohue Davis, was born on the Cave Spring Stock Farm, Jessamine County, Kentucky, on September 6, 1881, and died July 7, 1947. His father was a great great nephew of James Wilson, one of the signers of the Declaration of Independence, and Pennsylvania's first member of the United States Supreme Court. His mother was a great great niece of Daniel Boone, and a direct descendant of Oliver Cromwell.

Doctor Davis obtained his early education in the public schools of Jessamine County, Kentucky, and graduated with first honors in 1895. From 1898 to 1905 he took a special scientific course at Kentucky University, now Transylvania University.

He entered Jefferson Medical College in September 1906 and was graduated with honors in 1910. He served as an interne at the Jefferson Medical College Hospital for eighteen months. At the end of his internship he was awarded the Corinna Borden Keen Research Fellowship, and during the following year did research work in the laboratories of Professor Ludwig Pick of the University of Berlin, Germany, and in the Friedrichstein Krankenhaus. The result of this work was published in a monograph entitled "Development and Anatomy of the Nasal Accessory Sinuses in Man." He entered private practice in Philadelphia in January 1913, at which time he was appointed Clinical Assistant in Surgery at the Jefferson Hospital.

In 1931, with J. Parsons Schaeffer, he was awarded the Gold Medal, Class Two, for excellence of presentation of research illustrating embryology, development and anatomy of the paranasal sinuses, at the Annual Meeting of the American Medical Association in Philadelphia.

In 1936, he was made Clinical Professor of Plastic and Reconstructive surgery at Jefferson Medical College, and Maxillo-Facial Surgeon at Jefferson Hospital.

His professional career was outstanding for his work in harelip and cleft palate surgery, for which he received wide acclaim, both in this country and abroad. His contributions to the literature upon this subject are of particular note. He was first editor of the journal *Plastic and Reconstructive Surgery.*

During the First World War, Doctor Davis served on the War Department's Advisory Board of Pennsylvania, and later as a captain in the Army Medical Corps, in charge of the school of maxillofacial surgery. In the Second World War, he served as a member of the national faculty for plastic and maxillofacial surgery.

He received an honorary degree of Doctor of Science from the Georgetown College, Georgetown, Kentucky in 1933. He was president of the Alumni Association of Jefferson Medical College in 1942, and from 1941 to 1947 was a member of the Pennsylvania State Board of Plastic Surgery.

He was a fellow of The American College of Surgeons, The American Laryngological Society, The American Academy of Opthalmology and Otolaryngology, The American Society of Plastic Surgeons, The Association of Military Surgeons of the United States, The American Medical Association, and a past president of the American Society of Plastic and Reconstructive Surgery. He was a member of the Academy of Surgery of Philadelphia and the Philadelphia County Medical Society.

He was elected a Fellow of the College of Physicians November 1, 1916, and took an active part in the activities of this section; serving as its chairman in 1939 and 40, and as a mem-

* Read before the College of Physicians of Philadelphia's Section on Otolaryngology, 17 December 1947.

ber of the Executive Committee from 1941 to 1946. He was a member of the Hall Committee of the College from 1943 to 1947 and served as its chairman from 1945 to the time of his death.

Jefferson Hospital was his principal workshop, and those of us who knew him there will recall his enormous capacity for work, and the fine quality of the work which he did. A giant of a man, with commanding appearance, he was full of dynamic energy which he exerted tirelessly in his profession. His routine day's work, which he continued until his last illness, makes the average person feel tired to contemplate. He would appear on the sixth floor, where he had a special ward, at 7 A. M. to dress patients, following which he would operate until early afternoon. The remainder of the afternoon was spent in his office, after which he returned to the hospital to make rounds. This routine he continued through the years with but short intervals for vacation. It was an amazing thing to see this huge man carry out with remarkable skill and deftness, the delicate maneuvers necessary to repair a cleft palate in a few weeks old infant.

A fine tribute is given by a supervising nurse who worked with him for twenty-five years. "I found him to be a kind, conscientious, exacting, hard working man, good and kind to everyone."

In addition to his professional ability, the members of this section will recall with great pleasure the occasions upon which he entertained us at the Union League. He was a generous and gracious host, and those dinners revealed his keen appreciation of the fine art of delightful living.

Doctor Davis is survived by his wife, the former Ada Springer, whom he married in 1913, and four sons, Doctor J. Wallace, Warren S., J. Leslie and Richard E. Davis.

Annual Report on the Library*

Introduction

TEN years ago we began attempting in these reports to anatomize the library's functions, structure, and routines, so that there might be permanently available to those interested a sort of four-dimensional blueprint of this complex and elusive organism. There is no doubt in librarians' minds that theirs is one of the most misunderstood professions in the world. Employing procedures that are complex and sometimes highly technical, called upon for accuracy, for general and special knowledge, and for resourcefulness above the ordinary, too often even those serving the public most directly, and who have perhaps just pulled a reader's chestnuts out of the fire for him, are abashed by an explicit suggestion that there is no more to the librarian's job than taking a book off the shelf, stamping it, and handing it over to the reader. A library can help to win more understanding of the services it offers, one may suppose, if it consistently and patiently attempts to explain to its public what those services are and by what means they are provided. It is not a simple task to explain the laws and procedures of any profession to the layman, nor can one sensibly expect to achieve overnight a revolution by revelation. Yet there is every reason, in the readers' as well as the librarians' interest, to continue the work well into the night. We do not make converts by our silence.

In earlier reports will be found indications of what we conceive the library's functions to be, these being inevitably conditioned largely by the accumulations of the past, our relations to the local and national medical community, and by finances. Something has been said concerning the library's structure and its routines, involving the duties of various of the library assistants. The offices of the *Herr Direktor* have been mentioned lightly only to be dismissed as lightly. Yet, if the work of the assistants constantly and directly serving the public can be as casually regarded as it so frequently is, it must be supposed that there can be largely only total ignorance concerning the very existence of a pilot for the robot ship. Certainly there can be but little general knowledge of his duties, and it may therefore be of some interest to put them under the knife. A delicate operation under the circumstances, obviously, but one that will be performed as objectively as possible, with the understanding that the findings shall be regarded as theoretical only and that any resemblance between them and the parts of any one librarian, living or dead, shall be held as not only coincidental but downright miraculous.

Offices of the Librarian

Departmentalization clearly in itself implies the necessity of an overall authority to coördinate policies, supervise operations, and act as court of appeal. The Authority's duties become more rarified, of course, as the department staffs ascend the scale of excellence; but at no time do they completely vanish into the stratosphere. When, for any reason or combination of reasons—insufficient funds, bad judgement, poor organization, unfavorable market, etc.—the departmental staffs are not adequately manned for the work at hand, The Authority's duties scale down regularly from the sublime to the mundane.

Our library is departmentalized to the extent that one may recognize the following rough divisions of work enlisting the personnel under the immediate authority of the librarian: circulation, current periodicals, cataloguing, acquisitions, supporting services. It should be observed that there is no reference department as such, the librarian and the assistants attempting to meet the constant and varied demands of this sort as a not unpleasant addition to their routine duties.

* 1 November 1946–31 October 1947.

It is next in order to observe that this is a library containing 167,200 accessioned items and 321,240 unaccessioned items, in addition to the current volumes of 1,169 periodicals, covering the entire range of medical printing chronologically (and some of the manuscript period), with literature printed in Latin, Greek, Arabic, Chinese, Japanese, Russian, and all the major modern European languages; that this research collection is handled, under a budget quite inadequate to the potentialities of the collection, by a staff consisting (in addition to the librarian) of 1 combined assistant librarian and head cataloguer, one assistant cataloguer, 1 regular circulation assistant, 1 regular current-periodicals assistant, 1 secretarial and general assistant, and 3 pages, one of whom also provides photostat service. Let us now add that this is not a cloistered, scholar's library, open but a few hours a day to a select few, but one with two separated public rooms frequently more than filled to capacity with a heterogeneous group of practitioners, researchers, scholars, teachers, students, and a host of workers in miscellaneous allied fields, and that it is open a full day every weekday and two evenings a week.

There could obviously be no serious question of the need for an administrative librarian in a library of this size and scope and magnitude of use. But what abilities should he have to make the library of the greatest possible use to the readers within the inflexible limits imposed upon him by the sadly deficient funds at his disposal?

It will be convenient, and correct up to a point, to consider the librarian's sublime and mundane responsibilities separately, the latter first.

The selection of a staff is in our library, as in most others, a responsibility of the librarian. In making the selection he is governed by the usual factors operative in such matters—funds, available market, and personal judgement; and by the very special consideration that the library's collections are in highly specialized fields, with additional extraordinary linguistic demands. There is at present only an encouraging foreshadowing of selective training for medical librarianship, while the number of our citizens enjoying even a bowing acquaintance with a foreign language, dead or alive, unhappily steadily declines. The result is that the librarian with both medical library experience and linguistic facility is a rather rare bird, with all that that implies in the marts of trade. Since the library is unable to pay for a full corps of such rariora, the librarian must exercise particular judgement in the selection of assistants, to obtain, above all, those with native intelligence and the will to learn, accepting any additional abilities as so much manna from heaven. By the same token, the librarian, though he should have a knowledge of all the techniques employed in the various departments, must depend, in the light of his other responsibilities, upon an assistant librarian to teach procedures when that is necessary; to arrange schedules; in short, to keep the routine affairs of the household running in good order. When the assistant librarian doubles in brass, as ours does, performing also the highly technical duties of the head cataloguer, it may be seen that her job is no sinecure.

The librarian, then, will probably not take an active part in the routine functions of the staff. But he must keep himself steadily aware of what is going on, must be quickly accessible to suggestions or complaints from readers or staff, must be ever on the alert to learn of new procedures that might reduce the work of the staff and enable it to render greater service to the readers. To keep himself thus informed, he will require that, so far as possible, all incoming and outgoing library correspondence (other than routine notices) pass through his hands; he will make a point of using the facilities of the public rooms frequently, observing, listening, and, as occasion affords, indicating by example the spirit of interest in and helpfulness toward the readers that the staff is expected to maintain; he will study the methods and equipment of other libraries, in the libraries themselves when the opportunity offers, and as they are presented in the various

professional library journals and the advertisements of the library supply houses.

Personal review of the daily mail not only allows the librarian to keep informed of a large segment of the library's business, but serves as a short cut to the handling of it: decisions, reference questions, etc., that would have to be referred back to the librarian from the departments concerned are caught on the wing and settled with that much less loss of time. The library has, of course, a set of essential rules to govern the larger conduct of the library in relation to its users, and these provide a sturdy routine support for the assistants, harried by innumerable requests for special favors. To give them discretionary powers in the administration of the rules would subject them to pressures which would inevitably result in discomfort to them. And yet there are occasions when a rule should be waived. When an assistant believes the circumstances warrant, she refers the request to the librarian, who, against a larger framework of reference, is in a better position to make the decision needed and to give an explanation to the reader based on other factors than the printed rule. For many other matters requiring decision there are no rules at all, nor could there well be. Many such matters are brought to attention in one department of the library when they bear no conceivable relation to the specific work of that department or to any other of the departments, but represent, rather, a perhaps unprecedented chance to be of service. Decision as to whether the opportunity offered is to be accepted requires the sort of judgement based on experience, foresight, and overall knowledge of the library's proper functions that is properly to be expected of the librarian and unreasonably demanded of the assistants. In short, there is no department, no phase of the work of the library in which there does not arise daily the question beyond rule or precedent or individual capacity, that requires that extra bit of experience, authority, and knowledge that the librarian is there expressly to provide.

As has been indicated above, the library's dedication to a highly specialized and increasingly complex field, and the fact that its collections cover a world literature in time and language, make extraordinary demands on its staff. The less knowledge of the subject fields, the less linguistic facility, on the part of the staff, the greater the need for the librarian to supply the deficiencies. With the library unable to provide a rare book assistant, or a reference assistant with subject and linguistic experience, the librarian should be competent to handle the superficial demands of these fields, at least, if the corresponding collections, among the richest in the library, are to have any fair measure of use. Indeed, he should be able to pass easily from workaday correspondence in French, German, Italian, Spanish, Russian, the Scandinavian languages, and Dutch to locating a pathological description in the Latin of Morgagni, the Greek of an aphorism of Hippocrates, to the determination of a bibliographical variant, and on back to the location of an article on a subject vaguely described to him over the telephone, written by a Frenchman or a German sometime between the two World Wars probably, and which *may* have appeared in the proceedings of one of the international congresses and be unindexed.

One of the heaviest of the librarian's mundane responsibilities is that of seeing that there comes into the library, by purchase, gift, or exchange, the material proper to the library's status as both a practitioner's and a researcher's library, because the fellowship of the College includes both categories of physician. In addition, there are to be considered workers in allied fields for whom the library represents the sole reference source in the community.

The library's financial burden, and the librarian's work in this respect, are appreciably lessened by long-standing, cordial, and mutually advantageous relations with the city's outstanding group of medical publishers. But there remains a vast area of the literature not so easily disposed of.

After a century and a half or so of relegating to a sub-committee of the Library Committee the responsibility of selecting the material to be purchased, the Library Committee came to

the conclusion, about a decade ago, that a sub-committee of three specialists, annually subject to change in personnel, was less likely to have the long view and the wide view needed to increase the library's collections effectively than was the librarian, whose business it was to have an intimate knowledge of the collections and of the present and potential use of them. The librarian now, therefore, exercises the heavy responsibility of selecting the acquisitions by purchase, subject to post facto approval of the Library Committee. Whether or not he makes use of an advisory committee of specialists, he must stand on Olympus and keep a watchful eye on the course of events below, knowing that the Art is long, experience treacherous, judgement difficult, even with the aid of advisors. He will want to know, first, the strength and the weaknesses of the collections, both absolutely and in relation to other collections that may be available for use by the library's readers. He will want to have an intimate knowledge of the types of material asked for by the readers, and to be prepared to distinguish between legitimate and illegitimate demands, on the basis of proper function and adequate funds.

Since it would be chimerical, and unnecessary, to demand that the librarian have a specialist's knowledge of all the branches of the basic medical sciences and clinical medicine, let us say that obviously he might well bring to this particular task as rounded a subject knowledge as possible, without for a moment overlooking the primary fact that, basically, the art requires not so much subject knowledge *per se* as the librarian's technique: the ability to use languages, to uncover the most reliable sources of information, to retain and apply what one has read and heard, to keep the mind alert and ever inquiring. Few disciplines grow and foliate so restlessly as do the medical sciences. The librarian cannot operate, as the general practitioner can, secure in the possession of an armamentarium of knowledge acquired in five or six years of concentrated subject training, which he adds to only slowly as experimentation slowly evolves into proof and accepted practice; nor can he confine himself to a limited field, as the researcher does. His job is not to know how to diagnose, to treat, to experiment; but to know how and where to find quickly in the literature the information needed, and to see that so far as possible it is already in the library. He needs, basically, a wide-ranging and superficial subject knowledge capable of bridging the gap between the demands of the physicians and the researchers. The readers supply the team with most of the detailed subject knowledge; he provides it with the key to the literary storehouse in which are kept the assorted tools needed to apply and augment their knowledge most effectively.

This means that the librarian must studiously follow the current literature in its surface aspects, to a degree not usually indulged in by any one of the users of the library. He will have brought to him, as they come into the library, the current issues of the most representative of the journals in the major languages; he will carefully and promptly scan the unending announcements and catalogues of the publishers. He will be ever on the alert to catch from the library's users stray bits of information regarding work in progress or out-of-the-way publications, critical evaluations, that may be of extraordinary assistance to him in his selection of material. As indicated above, the broadest possible viewpoint must be taken that is consistent with intimate knowledge of the collections, the present and potential use of the library, and the funds available. He needs not only a working knowledge of the history of medicine—but the historical point of view.

The librarian is not only a worker in the library but its representative to the world at large. He should have the personal qualities and the general knowledge properly to be demanded of an official representative of a distinguished scientific or learned body. He deals with committees, and should be able to do so tactfully but frankly; initiate he must, in the nature of things, but it should be always within the framework of an unexpressed awareness that he is custodian and not owner. Entrusted

with large responsibilities, he must be scrupulously honorable and fair, placing the interests and good name of the library in the forefront of all his dealings on its behalf. He should be able to say 'no' to staff or readers with such judgement and in such spirit that the decision can be seen clearly to come not from the heart or the liver but from the head. He should be able to take it philosophically if an adverse decision, so conscientiously rendered, falls on fallow ground.

As one of the major medical research libraries, the library has an obligation to participate in the affairs of the local and national library associations. The librarian's interests should be broad enough to make natural and effective his participation in these affairs; and his administrative ability acute enough to make it possible without undue sacrifice of his primary duties.

This lengthy, but still far from complete, statement of desiderata will, it is hoped, serve as another panel in the picture of the library's organization that we are attempting to draw for the use of our contemporaries and those who will follow after us. Finally, it will perhaps be not inappropriate to suggest that, at this stage of the library's development, foolish indeed would be the librarian who measured himself against the potentialities of his job and did not find himself wanting. Let us, then, require also humility, ambition, good humor, good will.

The Past Year

The statistical part of our report, appearing below, makes abundantly clear that use of the library far surpassed not only the use made of it last year but also that in 1939, the last year before the war. All indices—attendance, circulation of books, inter-library loans, photostats supplied—point to a library with growing pains that belie its venerable age of nearly 160 years. The adjustments indicated are receiving the earnest attention of the Library Committee and the Council of the College.

There was some, though not complete, clarification of the foreign periodical situation. The missing volumes and issues of the war years were supplied in unexpected and most gratifying numbers by our Netherlands agent. The importance of getting this scarce material bound as soon as possible was immediately recognized, but payments for the material itself, and the greatly increased costs of binding, could not all be met out of the funds the library had carefully reserved for these purposes. An appeal to the Fellows met a generous response. And approximately 400 additional volumes were paid for and bound by means of a generous grant of $3,000 obtained by the president and other interested Fellows of the College from the American Philosophical Society. Thus, the library is one of the few to have this material available in viable condition.

There remains, however, the problem of volumes which we still lack either in their entirety or in part. Despite efforts on a national scale to obtain information as to the extent of Axis-dominated publications in the war years and to arrange for re-publication of exhausted stocks, not much appears to have been accomplished in a definitive way. Meanwhile, the incomplete, or supposedly incomplete, volumes, printed on poor paper, are rapidly deteriorating. Wherever possible, we are obtaining photostatic copies of issues that represent smallish lacunae in our files and having the volume bound. A further problem is the re-establishment of receipt of the current German journals. Our agent is not yet licensed to send to us many of these journals, but in the expectation that he soon will be, and because of the excellent service previously rendered in this complicated business, we have held off transferring the subscriptions to another agent who might possibly obtain a more immediate receipt.

It is a pleasure again to record a grant of $1,000 from the Smith, Kline & French Laboratories, made in recognition of the services of the library to their staff.

The library was selected as one of the 11 recipients of the 12-volume sets of reprints codifying the war work sponsored by the Com-

LIBRARY OF THE
COLLEGE OF PHYSICIANS
OF PHILADELPHIA

mittee on Medical Research of the Office of Scientific Research and Development.

There was perhaps no outstanding acquisition of an historical nature, but there were a number of more than passing interest. Among them, we may mention: 1) a medical receipt book compiled by Mrs. Joseph (Elizabeth Coates) Paschal (1702-c.1753), of Philadelphia. No dry compendium this, but a highly personalized little book that gives an entertaining picture of the domestic practice of medicine in this city in the first half of the 18th century. With this, a later receipt book, evidently based on Mrs. Paschall's and doubtless compiled by a kinswoman. Both were presented by Mrs. Francis Strawbridge, through our good friend Samuel Bradbury, M.D., shortly before his death; 2) an interesting letter (dated 24 Aug. 1805) on inoculation, written in familiar terms by Benjamin Waterhouse to Christopher Grant Champlin, of Newport, R. I. Presented by J. H. Cloud, M.D.; 3) an exchange of letters between Gen. W. C. Gorgas and James Thorington, M.D., who was in his early days a railway surgeon in Panama. Presented by J. Monroe Thorington, M.D.; 4) a manuscript in Latin, probably 18th century, entitled *De Auditu et Ejus Organo.* From the Estate of Thomas Scattergood; 5) Hollerius' commentary on the aphorisms of Hippocrates, Geneva, 1675. Presented by Alice Weld Tallant, M.D.; 6) a number of association items linked with the names of the British ophthalmologists Sir William Lawrence and the Critchetts, father and son, and with that of the donor, Burton Chance, M.D.; 7) Nathaniel Manning's matriculation card of 1803 signed by Shippen and Wistar, with his license to practice medicine in the State of New Jersey, 1804. Presented by C. H. Watson, M.D., through George Morris Piersol, M.D.; 8) Hiram Corson's "List of my expenses while a student of medicine," 1826-8. Presented by E. F. Corson, M.D.; 9) a recent series of Belgian medical postage stamps, with some French ones. Presented by G. N. J. Somner, M.D. It is not feasible, unfortunately, to itemize in this way all of the gifts of an historical interest that come to the library in a year's time, but such samplings, chosen more or less at random to illustrate types of material, serve to show that these collections are constantly being enriched through wise respecters of history who are also friends of the library.

In this connection, it should be observed that the William N. Bradley Collection was added to importantly during the year by its alert and generous donor; and that Dr. Samuel Sturgis was able towards the close of the library year to resume work on the Sturgis Collection. With the aid of these two collections, and others of the library's collections, we were able to contribute some rare and interesting historical material to the American Medical Association's celebration of its centenary, and to the annual meeting of the Association of Medical Illustrators.

The customary annual demonstrations of the contents and of an efficient use of the library were accorded the first year class of the Woman's Medical College and the Free Library's Training Class. And, for the first time, the teachers of the Division of Physical and Health Education of the School District of Philadelphia were formally introduced to the library. It is to be hoped that in time a way will be found to extend this practice to students in the other medical schools of the city and to other interested groups.

The chairman, Dr. Burton Chance, again represented the library at the annual meeting, at Montreal, of the Osler Library, of which, by virtue of his office, he is a curator.

There were a number of staff changes, as usual. Our assistant cataloguer, Mrs. Grant, resigned in July, for domestic reasons, and was succeeded by Miss Gertrude Cirotti. Miss Anne Ludovici, Mrs Emily Myers, and Miss Mary Tanaka, with us too briefly, were succeeded as pages by Miss Vilma Harmon and Miss Rose Massimi, while Miss Sally Kologiski happily continues as page and photostat operator.

The assistant librarian and head cataloguer, Miss Clara Manson, in addition to the discharge of her professional duties with the competence and selflessness that has long since won

the admiration of all, served on the Executive Board of the Special Libraries Council of Philadelphia, was a member of its Committee on Cooperation and its representative to the Adult Education Council, and was a member of the Medical Library Association's important Committee on a Training Program for Medical Librarianship. It would be impossible for the librarian to express adequately his appreciation of the head and hand work contributed by the assistant librarian and all the staff towards making use of the library a pleasure to the readers.

The librarian continued to serve as editor of the College's *Transactions & Studies*, and as secretary of the Hall Committee. He presided at the annual meeting of the Medical Library Association, at Cleveland, in May, and continued to serve on the Association's Committee on a Comprehensive, Coördinated Abstract Journal for Clinical Medicine. He was chairman of the Committee on Revision of the Constitution of the American Association of the History of Medicine, and continued as a consulting editor of the *Journal of the History of Medicine*. In March, he was a guest speaker at the Institute on Libraries held by the library of the New York Academy of Medicine as a part of the Academy's commemoration of its centennial anniversary; and, in October, gave an address at the annual dinner of the Association of Honorary Consultants to the Army Medical Library, in Washington. A paper based on these addresses appeared, under the title, "The Researcher, the Searcher, and Research", in the December, 1947, issue of the *Transactions & Studies*.

V. The library's roster, as currently constituted, follows:

Librarian

W. B. McDaniel, 2d

Assistant Librarian and Head Cataloguer

Miss Clara S. Manson

Assistant in Charge of the Reading Room

Mrs. Maud G. Maines

Assistant in Charge of the Periodicals Room

Mrs. Elizabeth F. Bready

Assistant Cataloguer

Miss Gertrude Cirotti

Secretary to the Librarian, and General Assistant

Miss Kathryn Haegele

Photostat Operator and Page

Miss Sarah Kologiski

Pages

Miss Vilma Harmon
Miss Rose Massimi

(*Continued on next page*)

Inventory

	1947	1946
Total number of accessioned[1] items	167,200	165,004
	1947	1946
Incunabula	415	415
Manuscripts (including a few typescripts)	677	653
General	166,108	163,936
	167,200	165,004
Total number of unaccessioned[1] items	321,240	320,665[2]
Reports	26,655	25,950
Periodicals "reserve"[3]	6,084	5,709
Theses and Dissertations	52,299	51,499
Pamphlets	236,202	237,507
	321,240	320,665[2]
Total number of current periodical publications regularly received	1,169[4]	1,258
Portraits[5]	66,081	63,802

Distribution of This Material

	Accessioned Items	Unaccessioned Items
General Library (including the Lewis Library)	162,965	321,236
On permanent deposit:		
Gross Library	3,818	4
Parry Library of the Obstetrical Society of Philadelphia	217	0
Mütter Museum[6]	200	0
	167,200	321,240

[1] Our 'accessioned item', or 'volume', normally contains not fewer than 100 pages, usually is bound, and always is catalogued. It may comprise a part of a 'book' or periodical 'volume', one or more complete 'books' or periodical 'volumes,' a collection of reports, pamphlets, or theses. In a few instances, the term applies to miscellaneous items such as a photograph album or a large collection of correspondence or private papers.

The 'unaccessioned item' is intended to apply to (usually unbound) pamphlets, reports, theses, or other material of fewer than 100 pages; only a part of this material is catalogued. It should be stressed, however, that in this category are included uncounted thousands of reports and theses of 100 pages or over, as well as smaller classic items, which would quite properly figure in the 'number of volumes' claimed by other libraries, and which would indeed figure among our 'accessioned items', had our predecessors and we ever been able to accession and catalogue them.

[2] Representing a deduction of 1,575 from the corresponding figure in last year's report, to accord with the elimination from the present report of the now meaningless item, "Complete and incomplete volumes of other periodicals not regularly received."

[3] More-or-less complete duplicate volumes of important and much-used periodicals.

[4] This figure does not include a large number of regular Western European subscriptions of which no current issues were received this year, but which were included last year on the basis of wartime issues received and the unfulfilled hope that the receipts would be continuous.

[5] Including 114 oil, and 426 other, framed portraits in the care of the Committee on College Collections. The count of portraits represents the number of entries on the cards in the portrait catalogue. The entries represent, in turn, both loose portraits and those in books, many of them, of course, being merely different reproductions of a single original.

[6] The books of the Mütter Museum are not permitted to be removed from the College building.

Current Periodicals

	Purchased	Exchange or Gratis	Annuals	Total
U. S. A.	244	314	34	592
Western European Continent	244	26		270
Latin America	25	89	1	115
United Kingdom and Eire	94	28	1	123
Canada	2	20		22
Eastern European Continent	6	5		11
Asia	7	9		16
Africa	1	8		9
Pacific Area	2	9		11
Grand Totals, 1947	625	508	36	1,169[4]
Grand Totals, 1946	753	479	26	1,258
Grand Totals, 1939	688	514		1,202

New titles: A total of 72 periodicals was added to the Norris Room in 1946–47. Sixty-three of these were purchased, 9 received in exchange or gratis. There were 57 that began with volume 1.

Separate Issues received, checked-in on the cards, and shelved totaled 11,725. In addition, thousands of duplicate issues were received, as usual; 375 of these were retained for our 'reserve' files, no attempt being made to count those held merely for exchange or other use.

Visitors to the Norris Room for the year totaled 5,764.

Readers' Use of the Library

Library Hours. There was no significant change in the library's hours during the year. It was open, during the academic year, from 9:30 to 9:30 on Mondays and Wednesdays; from 9:30 to 5:30 on the other weekdays. A closure of two weeks in August was again necessitated by repairs to the building which could not be made without rendering the library uninhabitable. During June, July, the rest of August, and the first half of September the library was open from 1 to 9:30 on Wednesdays; from 9 to 5 on the other weekdays, except Saturdays, when it was closed. The following legal holidays were observed: Thanksgiving (beginning at 5:30 the preceding evening), Christmas and New Year's (beginning at 1 on the preceding days), Memorial, Independence, and Labor Days.

Number of visitors:

	1947	1946	Totals 1947	1946	1939
Days (including evenings)	(289)	(284)	14,501	12,253	12,746

Circulation of books:

	1947	1946	1939
Number of volumes taken out	8,107	7,576	8,524
(Books: 3,218; Periodicals: 4,889)			
Number of volumes consulted in the library[7]	56,245	36,568	49,725

Inter-library loans: The library sent 1,813 (1946: 986) volumes on inter-library loan to 94 (1946: 80) libraries in 27 (1946: 20) States and has borrowed 2 (1946: 13) volumes from 1 (1946: 6) library.

Photostats: 3,752 photostatic prints were furnished on request (1946: 3,359).

Acquisitions and Accessions

Accessioned Acquisitions:

1947: 2,198 volumes (1,336 by purchase; 716 by gift; 146 by exchange). (Books: 923; Periodicals: 1,215).

1946: 1,979 volumes (1,020 by purchase; 701 by gift; 258 by exchange). (Books: 870; Periodicals: 1,109).

Non-accessioned Acquisitions[8]:

1947: 336 Pamphlets (1946: 130).
701 Reports (1946: 71).
800 Theses (1946: 2,917).

[7] The number of volumes "consulted in the library" includes only those supplied on demand. Readers have access to the bound volumes of periodicals and reference works kept on the shelves in the Reading Room; the Fellows, and occasionally others, by special permission, have access to the book-stacks. There are, therefore, many volumes consulted of which no accurate record can be kept.

[8] As usual, not all the pamphlets, theses, and numbers of various journals listed as received had been checked for keeping or discard at the close of the library year.

Donations

The individual donors for the past year number 317 (1946: 276). The library is indebted for large gifts of books, pamphlets, and unbound periodicals to the following donors:

Drs. H. P. Brown, Jr., K. Chouké; F. A. Davis Co.; Drs. W. A. N. Dorland, A. A. Eshner, C. Farr, L. E. Hunt, E. B. Krumbhaar, E. Larson; Lea & Febiger; Dr. W. E. Lee; J. B. Lippincott Co.; Dr. L. H. Mutschler; J. Paton, Pennsylvania Hospital, Philadelphia Bibliographical Center, Rockefeller Foundation, W. B. Saunders Co., Union Library Catalogue; Dr. J. Walsh (Estate); Dr. I. J. Wolman; Woman's Medical College, Wyeth, Inc.

Various publishing houses have presented volumes as follows: Blakiston Co., 5; F. A. Davis Co., 24; Lea & Febiger, 22; J. B. Lippincott Co., 37; W. B. Saunders Co., 51.

Other individual donors were as follows: Drs. A. A. Aballi, L. C. Abbott; Lt. Col. A. H. Adams; Drs. A. S. Alving, M. Asbell, W. S. Bainbridge, E. S. G. Barron, S. Bellet, A. Benchetrit, E. S. Bereston, A. H. Blakemore, S. W. Boggs, W. G. Bowerman, S. Bradbury, W. N. Bradley; Mrs. E. F. Bready; Drs. C. C. Burlingame, W. W. Cadbury, M. Carmack, B. Chance, J. Cooke, A. C. Cope, V. Z. Cope, E. Corson; Miss M. R. Crowe; Drs. H. Davis, J. Dean-Throckmorton, J. L. Despert, J. C. Doane, G. G. Duncan, J. H. Farrell, F. Fenton, E. B. Ferris; Mr. M. J. Fleisher; Drs. J. F. Fulton, J. G. Gibson, A. C. Giese, R. L. Gilman, A. Goldberger, H. I. Goldstein, F. M. Groedel, H. N. Harkins, E. N. Harvey, C. A. Hatfield, G. Hinsdale; E. B. Hodge (Estate); Drs. E. F. Horine, C. D. Hurd; Mr. & Mrs. D. G. Hyde; Drs. C. L. Jackson, M. S. Jacobs, W. A. Jeffers, V. E. Kinsey, J. V. Klauder, W. H. Kneedler, E. F. Knipling, W. E. Krewson, 3rd, P. R. Leberman, B. B. V. Lyon, A. Marques, B. Masuda, J. McFarland (Estate); Drs. W. D. Miles, O. H. W. Mitchell, F. Montaro; Dr. & Mrs. S. Mudd; Miss M. V. Naylor; Drs. H. Neurath, J. T. Nicholson; Miss J. Oppenheimer; Drs. G. W. Outerbridge, K. E. Paschkis, J. R. Pawling, O. H. P. Pepper, W. H. Perloff, H. Pleasants, Jr., G. Podio; Miss C. Raspondi; Drs. W. S. Reese, B. Riegel, R. F. Riley, H. C. Ruche, P. J. Sartain (Estate); Mr. L. Saunders; Drs. J. P. Schaeffer, B. Shankman, G. Siffert de Paula e Silva, H. E. Sigerist, F. W. Sinkler, C. N. Smith, L. H. Smith, H. R. Snyder, G. N. J. Sommer, G. N. J. Sommer, Jr., W. M. Stanley; Mrs. F. R. Strawbridge; Drs. E. A. Strecker, A. W. Tallant, E. W. Thomas, J. M. Thorington, L. Thorndike, H. J. Tumen, J. B. Vander Veer, H. R. Viets, W. S. Wadsworth; Prof. J. H. Watkins (through Dr. D. M. Pillsbury); Drs. C. H. Watson, M. B. Wesson, A. S. Wiener, DeF. P. Willard, P. F. Williams, A. C. Wood, G. B. Wood, W. Zentmayer.

Exchanges

The *Transactions & Studies* was sent, either as gift or in exchange, to 304 organizations. The library received a number of journal issues through the Medical Library Association Exchange.

Theses and dissertations to the number of 800 have been received on exchange from the following European schools of medicine: Universities of Amsterdam, Basel, Bern, Copenhagen, Göttingen, Heidelberg, Lausanne, Leiden, Louvain, Lund, Paris, Utrecht.

Work of the Cataloguers

	1947	1946
Accessioned items catalogued or recatalogued	842	892
Unaccessioned pamphlets and Fellows' reprints catalogued by author or by author and subject	1,359	965

Approved:
Burton Chance
Chairman

W. B. McDaniel, 2d
Librarian

Annual Reports of the Committees of the Mütter Museum and College Collections

The Museum

Activities

The museum was open weekdays from 10:00–1:00 and from 2:00-5:15 except Saturday when it was open from 9:30–1:00.

There were 1083 visitors during the year, the increase of 201 being due to the visits of the students from the Dolan College of Embalming and from the Pennsylvania State College of Optometry, to whom the task of writing a paper on the Mütter Museum has been assigned.

Dr. Ralph Pemberton again used Museum specimens to illustrate a lecture on lesions of arthritis.

Part I of the Catalogue of the Mütter Museum was published in the issue of the *Transactions & Studies* of the College dated June, 1947, and the remaining installments will appear in subsequent issues.

Mrs. Ella N. Wade was reappointed Curator and Clerk-Technician for the year 1946–1947.

Accessions

Presented by Mrs. David Hunt Ludlow, of Easton, Pa., from the estates of her late husband, Dr. David Hunt Ludlow, and his father, Dr. J. R. Ludlow, the following instruments:

Binaural stethoscope
Alison's binaural stethoscope
Dennison's binaural stethoscope
Percussor
Part of a phonendoscope
Urethrotome
Kelly's urethral calibrator
Catheters and mandrins
3 Fowler's sounds
3 probes
Catheter holder
2 Leur's trachea cannulae
Denhardt's mouth gag
Probang for larynx
Combination cheek retractor and tongue depressor
Rectal speculum
Pratt's trivalve rectal speculum
Screw driver for adjusting eye glasses
Critchett's eye speculum
Canaliculus knife
Politzer's aural forceps
4 artery forceps
Splinter forceps
Dieffenbach's curved artery forceps
Bullet forceps
Spring lancet
Dissecting tenaculum
Needle holder
Scarificator
Tampon expeller
Tooth extractor
Vectis and blunt hook
Perforator
Guarded crotchet
Hodge obstetrical forceps
Combination curette, hook and forceps
Péan's hysterectomy forceps
Ricord's vaginal speculum
Grave's vaginal speculum
Nott's vaginal speculum
Sim's dilating speculum
Seiler's septometer
Straight nasal saw
Sajous' angular nasal saw
Postnasal syringe
2 abdominal trocars
1 Cornet's cover glass forceps
2 Kuehn's cover glass forceps
Triangular bistoury
Torsion forceps
Iris scissors with probe point

The College Collections

Activities

Oil portraits and other framed pictures were cleaned and all wires checked and replaced where necessary.

Mrs. Ella N. Wade was reappointed Custodian and Clerk-Technician for 1946–1947.

Accessions

Presented by Dr. Edward F. Corson:
- Six British War Medals
  - St. John Ambulance Brigade (for coronation, 1911)
  - St. John Long Service and Good Conduct Medal
  - Crimea, 1854, with bars, Alma, Inkermann, Sebastapool
  - Turkish Crimea
  - Queen's South Africa Medal, 1901, with bars, Cape Colony, Paardeberg, S. A.
  - Naval Sick Berth, Long Service Medal
- Five British War Medals on a single bar
  - Military Cross and bar
  - British War Medal (1914–1918)
  - Victory Medal with Oak Leaf for "mention"
  - India General Service Medal with bar, Waziristan (1921–24)
  - George V Jubilee Medal 1835

Presented by Dr. Burton Chance:
- Four cataract knives formerly belonging to Dr. Douglas Hall
- Amputation set formerly belonging to Dr. Thomas H. Fenton
- Case of ophthalmic instruments brought from France by Dr. Thomas M. Drysdale and later given to Dr. Thomas H. Fenton
- Cataract knife devised by Jäger and used by the late Dr. B. Alexander Randall
- Spring-action scissors devised by Dr. Edward Jackson and used by him in operation on eye muscles
- Cataract knife devised by Dr. Edward Jackson and used by him
- Cataract set formerly belonging to Dr. Sartain
- Double-edged knife and scalpel formerly belonging to Dr. Thomas H. Fenton
- 2 Schwerger cataract knives formerly belonging to Dr. Thomas H. Fenton
- Trephine Set

Presented by Dr. Irving J. Wolman:
- Buttons worn by officers of the U. S. Public Health Service during World War II
- Medal of the Fifth International Pediatric Congress, N. Y., 1947
- Medal of 1st Pan-American Congress of Pediatrics, Washington, D. C., 1947

Presented by Miss Virginia Walker:
- Lead nipple and lead top to feeding bottle

Presented by Ch. F. L. Nord, President of the Ivory Cross Expedition, through Dr. Edward B. Krunbhaar, as a token of appreciation and gratitude for what the United States has done for the Netherlands after the war:
- Delft platter commemorating the Ivory Cross Expedition to Holland in 1946.

Presented by Mrs. Elizabeth Bready:
- Sigma Xi emblem formerly belonging to her father, Erwin F. Faber.

Presented by Miss Catherine Nick through Dr. Herman Beerman:
- Clock formerly belonging to Dr. Joseph Walsh

Presented by Dr. J. Monroe Thorington:
- Two medals
  - "Award of Merit Exhibition" to J. Monroe Thorington, M.D., by American Physicians Art Association, 1944 and 1946.

Oscar V. Batson
Chairman

Annual Report of the Publication Committee

This report covers the four numbers of the *Transactions & Studies* published within the College's fiscal year, ending 10 November 1947; namely, vol. 14, nos. 3 and 4, and vol. 15, nos. 1 and 2.

The total number of pages was 186, an increase of 24 over the number of pages in the preceding four numbers. The increase is in part accounted for by the fact that, beginning with vol. 15, no. 1, we were able to revert to our pre-war type-sizes, which reduce somewhat the amount of material that can be got on a page, but increase importantly the legibility of the text.

It is gratifying to report that, of the eight combined College and Philadelphia County Medical Society lectures, which may properly be regarded as the backbone of our publication structure, only one, that of Prof. John de J. Pemberton, was unavailable for publication. The utmost coöperation was manifested by the County Society in giving us access to the lectures which they had provided; and, in turn, they were given equally friendly access to the papers that fell under the College's jurisdiction.

The clerk of the College's Section on General Medicine, William G. Leaman, Jr., M.D., continuing the helpful practice of his predecessor, provided the committee with the full text of a number of valuable papers and with abstracts of the others.

In general, it may be observed that the scientific papers published in the four numbers under review presented highly authoritative statements on subjects of perennial or currently extraordinary interest to physicians and surgeons. In addition, the December, 1946, number received exceptional attention from medical historians by virtue of the papers on Benjamin Rush by Prof. Shryock, Dr. Pepper, and Mr. Gibson.

Printing of the catalogue of the Mütter Museum, as compiled by the curator under the supervision of members of the Museum committee, was begun in the last of the four issues. The publication of the catalogue, which will extend over a number of issues, is regarded as a major project that should considerably enhance the knowledge and usefulness of one of the College's outstanding departments.

Further interest in this series of numbers of the journal was lent by the printing in them of the proceedings of the Pathological Society of Philadelphia. As the Society has for many years held its meetings at the College, and there are many historical and contemporary links between the two bodies, it is believed appropriate, as well as mutually advantageous, for the College to provide a place in its journal for the proceedings of this closely affiliated society.

Financial Summary

Receipts

Appropriation	$1,000.00	
Additional appropriation	220.00	
Income from Publication Funds	675.99	
Sales and reprints	117.59	
Pathological Society of Phila.	69.00	$2,082.58

Expenditures

Printing and mailing	$1,894.96	
Secretarial services	40.00	
Postage	5.00	1,939.96
Balance		$142.62

Approved:

W. B. McDaniel, 2d
Editor

Samuel B. Hadden
Chairman

Annual Reports of the Sections*

General Medicine

There were seven meetings of the Section during the year, one held jointly with the Philadelphia Urological Society and the American Urological Association.

The membership increased slightly, from 144 to 148.

William G. Leaman, Jr.
Clerk

Medical History

There was no meeting of the Section in 1947, but late in the year the officers and executive committee held a meeting at which plans for reestablishment of the Section early in 1948 were discussed, and the following officers elected to serve during the period of reorganization: William G. Leaman, Jr., *chairman*, Maurice S. Jacobs, *clerk*.

The Section has been requested to act as host for the annual meeting of the American Association of the History of Medicine, to be held in this city in May, and it is expected that it will do so.

William G. Leaman, Jr.
Clerk

Ophthalmology

The total paid membership of the Section is now 58. Seven meetings were held during the year, with an average attendance of 81.

The tenth annual de Schweinitz Lecture was delivered by Dr. Bernard Samuels, of New York, on November 20th.

The Zentmayer Prize was awarded to William M. Hart, Ph.D., for his paper, "Hydration Properties of Excised Cornea and Factors Responsible for Transparency", presented on October 24th, 1946.

George F. J. Kelly
Clerk

* The programs of the Sections appear in the June and February numbers of the *Transactions & Studies*.

Otolaryngology

The first four of the six meetings in 1947 were held in collaboration with the Philadelphia Laryngological Society, the Section conducting those in February and April. The arrangements with the Philadelphia Laryngological Society to alternate monthly meetings terminated with the April meeting. The Executive Committee decided that no meeting should be held during October because of the conflict with the Academy meetings in Chicago.

The present membership of the Section consists of 4 Honorary Fellows; 57 Active Fellows. The average attendance at the meetings was 61: 23 Fellows, 38 guests.

During 1947 the Section lost by death Dr. Warren B. Davis and by resignation Dr. Harry Rothrock. Two new Fellows were elected, namely, Dr. F. Johnson Putney and Dr. J. J. O'Keefe.

Louis H. Clerf
Clerk

Public Health, Preventive and Industrial Medicine

There were three meetings during the year, with an average attendance of 45.

The total membership in the Section is 28; paid membership, 25.

P. F. Lucchesi
Clerk

Transactions of the Sections

SECTION ON GENERAL MEDICINE

26 May 1947[1]

PHYSIOLOGICAL AND SURGICAL IMPLICATIONS OF DISTURBED RENAL FUNCTION. Homer W. Smith*, M.D. (*Annual B. A. Thomas Oration of the Philadelphia Urological Society.*)

27 October 1947

THE BILIARY EXCRETION OF BROMSULFALEIN AS A TEST OF LIVER FUNCTION IN A GROUP OF PATIENTS FOLLOWING HEPATITIS OR SERUM JAUNDICE. C. Wilmer Wirts, M.D. (*Abstract 1, below.*)

CARONAMIDE: A NEW ENHANCING AGENT FOR USE IN CONJUNCTION WITH PENICILLIN THERAPY. William P. Boger*, M.D. (Printed in the *Transactions & Studies*, vol. 15, no. 3, December, 1947.)

PENICILLIN PLUS CARONAMIDE IN THE TREATMENT OF SUBACUTE BACTERIAL ENDOCARDITIS. J. B. Vander Veer, M.D., and F. MacD. Richardson*, M.D. (Printed in the *Transactions & Studies*, vol. 15, no. 3, December, 1947.)

CAUSALGIA IN ARTERIOSCLEROSIS AND THROMBOANGIITIS OBLITERANS: TREATMENT WITH TETRAETHYLAMMONIUM CHLORIDE. Meyer Naide, M.D. (*Abstract 2, below.*)

24 November 1947

RADIOACTIVE IODINE IN TREATMENT OF THYROTOXICOSIS. Karl E. Paschkis, M.D., A. Cantarow, M.D., and Th. Eberhard*, M.D. (*Abstract 3, below.*)

STUDIES ON ALLERGY TO TUBERCULIN IN STUDENT NURSES. Richard T. Ellison, M.D. (*Abstract 4, below.*)

THE CONCEPT OF INACTIVE HYPERTENSION, WITH SPECIAL REFERENCE TO THIOCYANATE THERAPY. J. Q. Griffith, jr, M.D., M. A. Lindauer, M.D., R. L. Shanno*, M.D., and Ella Roberts, M.D. (*Abstract 5, below.*)

ASPIRIN POISONING, WITH NOTES OF A FATAL CASE. Mitchell Bernstein, M.D., and Sidney O. Krasnoff*, M.D. (*Abstract 6, below.*)

[1] Combined meeting with the Philadelphia Urological Society and the American Urological Association.
* *By invitation.*

SECTION ON OPHTHALMOLOGY[2]

23 October 1947

MEMOIR OF DR. WALTER I. LILLIE. Glen G. Gibson, M.D.

CASE OF RETINOBLASTOMA CURED BY RADON. Charles E. G. Shannon, M.D., and Joseph Waldman, M.D.

PTOSIS OPERATION—FRIEDENWALD TECHNIQUE. (Moving Picture Demonstration.) Edmund B. Spaeth, M.D.

BILATERAL PAPILLOEDEMA ASSOCIATED WITH INFECTIONS OF THE NERVOUS SYSTEM. Joseph C. Yaskin, M.D., Robert A. Groff, M.D., and Henry Shenkin*, M.D.

20 November 1947

NECROSIS OF INTRAOCULAR TISSUES. Bernard Samuels*, M.D. (*The tenth annual de Schweinitz Lecture.*)

18 December 1947

FURTHER NOTES ON CASE OF ORIGINAL MIXED CELL TUMOR OF LACRIMAL GLAND. I. Edward Rubin*, M.D.

TERATOMA OF THE ORBIT: CASE REPORT. Fred Harbert*, Capt., MC, USN.

STUDIES ON FUSION. Edwin Tate*, M.D.

MASS SURVEY FOR DETECTION OF GLAUCOMA: A PRELIMINARY REPORT. Carroll R. Mullen, M.D.

SECTION ON OTOLARYNGOLOGY[3]

19 November 1947

PRIMARY CARCINOMA OF TRACHEA. William A. Lell, M.D.

[2] The presentations at this Section are customarily abstracted in the *American Journal of Ophthalmology* and the *Archives of Ophthalmology*.

[3] The presentations at this Section are customarily abstracted in the *Archives of Otolaryngology*.

Hemangioma of Ear and Mastoid Process. M. Valentine Miller, M.D.

Prevention of Anoxia following Tracheotomy. (Motion Picture.) Joseph P. Atkins, M.D.

17 December 1947

Memoir of Warren B. Davis, M.D. Austin T. Smith, M.D.

Examination of the Nasopharynx. Oram R. Kline, M.D.

Benign Tumors of the Nasopharynx. Karl M. Houser, M.D.

Chondroblastoma of Nasopharynx. William Hewson, M.D.

Carcinoma of Nasopharynx. C. Calvin Fox, M.D.

SECTION ON PUBLIC HEALTH, PREVENTIVE AND INDUSTRIAL MEDICINE

6 October 1947

The Problem of Chronic Illness. Philip D. Bonnet*, M.D.

Community Ramifications of Chronic Illness. Mildred V. Lucka*, R.N.

Nursing Needs in Chronic Illness. Marion E. Shand*, R.N.

The Chronic Invalid. Edward L. Bortz, M.D.

8 December 1947

The Importance of Good Public Health. E. R. Coffey*, M.D.

Abstracts

Abstract 1

The Biliary Excretion of Bromsulfalein as a Test of Liver Function in a Group of Patients following Hepatitis or Serum Jaundice. C. Wilmer Wirts, M.D.

Prolonged or permanent impairment of liver function is now known to occur in a variable proportion of patients following an attack of infectious hepatitis. However, the incidence of this chronic hepatic disease is not well established, because of the difficulty in correlating symptomatology with the available liver function tests and even liver biopsy.

The present report deals with an evaluation of liver function by means of the biliary excretion of bromsulfalein in a selected group of post-hepatitis patients. Twenty-five patients convalescing from hepatitis were selected because prolonged liver functional impairment was suspected, but not proven, on the basis of symptoms or slight abnormalities in the routine liver function tests.

The biliary bromsulfalein test has been previously described and consists of measuring the excretion in the bile of intravenously injected bromsulfalein.

All of the twenty-five patients showed impaired liver function on the basis of the initial biliary bromsulfalein test. On the basis of the same test liver function returned to normal in fifteen or sixty per cent of the patients when intensive therapy was continued for at least three months, while ten or forty per cent continued to show the hepatic functional impairment beyond this period.

It is felt that this test should be of help in evaluating liver function in selected patients in whom minimal hepatic impairment is suspected, particularly those patients with a history of having had hepatitis.

Abstract 2

Causalgia in Arteriosclerosis and Thromboangiitis Obliterans: Treatment with Tetraethylammonium Chloride. Meyer Naide, M.D.

The term causalgia has been used for certain painful states resulting from nerve damage following trauma and inflammation. A definition of causalgia as we use the term here is that it is a painful state arising from a focus of nerve irritability resulting from nerve damage or injury. One of the characteristics of the causalgic state is the response of the pain to sympathetic ganglion block, either temporary or permanent. It is the purpose

of this paper to point out that ischemia may produce a type of nerve damage that will result in the setting up of a causalgic state.

We have used tetraethylammonium chloride in 68 patients with arteriosclerosis and thromboangiitis obliterans. Relief of rest pain and claudication occurred in both conditions in some patients. Frequently improvement of symptoms occurred with a dose of tetraethylammonium chloride insufficient to produce vasodilatation. Since the relief of pain did not appear to be due to increase in blood flow the answer seems to be that we were relieving a causalgic state resulting from nerve ischemia similar to the manner in which causalgia is relieved when it is produced by inflammation or trauma. It must be remembered, however, that ischemic pain in many patients is made up of a number of components of which causalgia may be one. The dose of tetraethylammonium chloride must be individualized particularly in those with evidence of coronary or cerebral arteriosclerosis or hypertension. Elevation of the legs aids in preventing the hazardous drop in blood pressure that may occur in some patients with tetraethylammonium chloride. The use of tetraethylammonium chloride does not obviate the need for sympathectomy in some patients with severe ischemia.

Abstract 3

Radioactive Iodine in Treatment of Thyrotoxicosis. Karl E. Paschkis, M.D., A. Cantarow, M.D., and Th. Eberhard, M.D.

The basis for the use of isotopes in biological work is the fact that the cells of the body cannot distinguish between isotopes. Thus if one of the radioactive isotopes of iodine is administered as sodium iodide, the radioactive compound is taken up by the thyroid gland, molecular iodine is liberated, and within the thyroid cells incorporated in the thyroid hormone. A radiation emitter is thereby planted within the thyroid cells.

Of the various radioactive isotopes of iodine, I-131 is now available from the atomic stockpile in Oak Ridge. Its half life is eight days. It is a beta- and gamma ray emitter.

This report deals with preliminary experience with the use of I-131 in 10 cases of thyrotoxicosis.

All ten cases showed considerable improvement, nine of them clinical cure. The doses employed empirically varied from 30 to 3 mC. It is our impression that the smaller doses are equally effective. One case developed myxedema, necessitating the use of thyroid medication. Otherwise no serious side effects were noticed. One patient developed fine petechiae on the day of administration, which disappeared within 24 hours. The blood count, including platelet count, was normal. Two patients developed aphonia of 2 to 3 days duration; laryngoscopic examination showed reddening of tracheal and laryngeal mucosa.

Three of the patients were "thyrocardiac," elderly women who would have been a very poor surgical risk. Three patients had been treated previously with thiouracil and had not tolerated the drug.

The use of radioactive iodine in treatment of diffuse toxic goiter is promising, but no final evaluation is possible at this time.

Abstract 4

Studies on Allergy to Tuberculin in Student Nurses. Richard T. Ellison, M.D.

It was the belief of the earlier phthisiologist that once the body had developed a hypersensitivity to tuberculin the condition remained demonstrable for the rest of that individual's life. And up to twenty years ago that belief was correct in most instances because the population was so heavily tuberculinized that few could escape infection heavy enough or frequent enough to persist, even though latent, for life. More recently there has been a reversal of this opinion due to the fact that the incidence of open tuberculosis has been greatly reduced among the people of the United States and several other countries.

It is now recognized that many minimal lesions heal so completely that all tubercle

bacilli eventually die and are destroyed. Even the calcified lesions of healed tuberculosis are, in many instances, bacteriologically sterile. With the death of all tubercle bacilli the stimulus for the production and maintenance of both hypersensitivity and acquired resistance is removed and these mechanisms begin to diminish in intensity, allergy disappearing in a matter of a few months whereas acquired resistance may persist for years.

In many quarters, however, the truth and significance of these facts has not been appreciated and this has led to a misinterpretation and a misunderstanding of the significance of a negative tuberculin reaction.

If hypersensitivity were the only result of infection, its loss would leave all negative reactors entirely similar. The fact, however, that acquired resistance persists after allergy disappears makes it necessary to divide all negative reactors to tuberculin into two categories, those in the state of primary negative allergy and those in the state of secondary negative allergy with residual acquired resistance.

Since there is no clinical test for residual acquired resistance we must depend on other means of separating negative reactors into the two classifications. The only proof that a currently negative tuberculin reaction belongs in the secondary negative group is a history of previously positive allergy. Presumptive evidence, however, can be obtained from a careful study of X-ray films of the chest and from the physical examination of the lungs and thoracic cage for hypoventilation, retraction of the apex and atrophy about the shoulder girdle.

This method of classification was applied to a group of student nurses on admission to training. They had tuberculin tests at six months intervals and were reclassified on graduation.

This study shows that:

There was a yearly increment of students, originally negative who became positive reactors during training. Some were found positive for the first time only on graduation.

Many of those who became positive did not remain so but after a variable time reverted to a state of negative allergy.

If those originally negative to tuberculin were divided into primary and secondary negative groups it was found that:

Of the primary group a greater percentage remained negative to graduation but if they did acquire an infection they tended to retain their hypersensitiveness.

The secondary negative group tended to develop a positive allergy again at an earlier period than the primary negatives. This was attributed to the anamnestic response to reinfection and not to greater susceptibility. They tended to lose this reanimated allergy quite quickly so that allergy fluctuated during their three years of training. Fewer of them were still negative at graduation. None of those infections and reinfections were severe enough to be demonstrable by routine X-ray and none of them had symptoms or any illness attributable to tuberculosis.

Abstract 5

THE CONCEPT OF INACTIVE HYPERTENSION, WITH SPECIAL REFERENCE TO THIOCYANATE THERAPY. J. Q. Griffith, jr, M.D., M. A. Lindauer, M.D., R. L. Shanno, M.D., and Ella Roberts, M.D.

The concept is advanced that hypertension may persist after the initial cause has disappeared, and to this condition the term inactive hypertension has been applied. While the 'active' phase may not be identified with complete accuracy by the means now available, it is felt an approximate classification can be made by tests demonstrating abnormality of the kidney, pituitary, and capillary wall. In certain instances therapy may reduce the 'active' to the 'inactive' phase, which we have called 'secondary inactive' as compared with the initial or 'primary inactive' type. 'Active' hypertension seldom responds favorably to thiocyanate therapy, while 'inactive' hypertension, both primary and secondary, usually does. Death occurs less frequently in the inactive than in the active phase.

A parallel with animal experimental hypertension is drawn, and the possible role of diminution of the capillary bed in maintaining the hypertension is discussed.

Abstract 6

ASPIRIN POISONING WITH NOTES OF A FATAL CASE. Mitchell Bernstein, M.D., and Sidney O. Krasnoff, M.D.

Aspirin poisoning in the United States is rare compared to its incidence in Europe. Reports of only 7 fatal cases were found in the American literature, 2 of which were due to allergy.

The dose of aspirin producing toxic symptoms varies with the age, weight and physical condition of the individual. As little as 2 Gm. caused toxicity in elderly arteriosclerotic patients, whereas 85 Gm. have been ingested with recovery.

Aspirin is absorbed by all portions of the gastrointestinal tract, distributed among all the tissues and fluids in the body, and is eliminated through the kidneys. By its action upon the central nervous system, liver and kidneys, aspirin produces a clinical picture protean in nature, but strikingly similar in all of the cases reported. Weakness, headache, dizziness, vertigo, nausea, vomiting and diarrhea are soon followed by tinnitus, deafness and visual disturbances. Excitation producing restlessness, incoherent speech, mania, delusions, etc. occur and are referred to as the "salicylic jag". Finally, the picture is one of central nervous system depression consisting of coma, rapid shallow respirations, cyanosis and convulsive seizures. The marked hepatic and renal damage is manifested by petechiae and all the signs of a renal acidosis. This is confirmed by increased blood urea nitrogen, low CO_2 combining power, prolonged prothrombin time and marked urinary changes.

Our patient was a man 54 years of age, who ingested 75–100 grains (5.0–6.6 Gm.) of aspirin in 3 hours in order to relieve a severe headache. This was followed by a clinical picture similar to that described. The patient died about 24 hours after taking the drug. The diagnosis was confirmed by post-mortem findings of brain degeneration, petechiae over the skin and serosal surfaces of the body and marked hepatic and renal damage, together with detection of acetylsalicylic acid in the stomach contents and the post-mortem blood.

The treatment of aspirin poisoning is non-specific. Lavage and fluids as well as vitamin K are advocated.

An attempt is made to stress the fact that many instances of aspirin toxicity are being overlooked because of the apparent failure to recognize the early symptoms and signs, or because these symptoms and signs often mimic other disease entities i.e. diabetic acidosis, renal disease, encephalitis, frank psychoses, and blood dyscrasias.

After this paper was prepared, another fatal case of aspirin poisoning occurred on the Pediatric Service of Dr. Robert Schless at the Jewish Hospital. This was a case of a 5 month old white boy who was given 2 Gm. of acetylsalicylic acid in a period of 10 hours and died in a state of acidosis. The post-mortem findings were similar to our case.

List of the College Lectures, 1947*

8 January 1947

PEMBERTON, JOHN DE J. Management of Diverticulitis of the Sigmoid Colon. (*Not made available for publication.*)

5 February 1947

MINOT, GEORGE R. The Diagnosis and Treatment of the Macrocytic Anemias (*Nathan Lewis Hatfield Lecture XXXI*). (*Transactions & Studies*, April, 1947.)

12 March 1947

CECIL, RUSSELL L. Present Day Treatment of Arthritis. (*Transactions & Studies*, April, 1947.)

2 April 1947

GROSS, ROBERT E. Surgical Treatment for Cardio-vascular Malformations (*Mary Scott Newbold Lecture LVII*). (*Transactions & Studies*, June, 1947.)

1 October 1947

HARTMAN, FRANK W. Studies on the Pathology and Prevention of Anoxia. The Methods for and Clinical Application of Continuous Recording of Blood Oxygen (*Mary Scott Newbold Lecture LVIII*). (*Publication delayed.*)

5 November 1947

ARONSON, JOSEPH D. The Evaluation of BCG Vaccine in the Control of Tuberculosis (*Alvarenga Prize Lecture VII*). (Scheduled for publication in the *Transactions & Studies*, April, 1948.)

3 December 1947

SMILLIE, WILSON G. The Physician's Role in Preventive Medicine (*James M. Anders Lecture XXII*). (*Not made available for publication.*)

* The meetings from January through April were held jointly with the Philadelphia County Medical Society, which arranged for the January and March ones.

Fellows

December 31, 1947

ELECTED

1912. Addison, William H. F., Medical Laboratories, Univ. of Pa.
1926. Adler, Francis Heed, 313 S. 17th St.
1914. Aiken, Thomas G., Berwyn, Pa.
1936. Aldridge, Fred Cutler, Wayne, Pa.
1936. Alexander, Fay Knight, Fitzgerald Mercy Hospital, Darby, Pa.
1947. Allbritten, Frank F., Jr., 1025 Walnut St.
1906. Allen, Francis Olcott, Jr., 2216 Walnut St.
1932. Allen, Frederick H., 1711 Fitzwater St.
1935. Alpers, Bernard J., 111 North 49th St.
1905. Anspach, Brooke M., 1827 Spruce St.
1930. Appel, Kenneth E., 111 N. 49th St.
1905. Appleman, Leighton Francis, 308 S. 16th St.
1935. Armitage, George L., 400 E. 13th St., Chester, Pa.
1922. Arnett, John H., 2116 Pine St.
1942. Aronson, Joseph D., Henry Phipps Institute, 7th and Lombard St.
1920. Astley, G. Mason, 812 N. 63rd St.
1944. Atkins, Joseph P., 1201 Knox Rd., Wynnewood, Pa.
1935. Atlee, John L., 37 E. Orange St., Lancaster, Pa.
1935. Atlee, John L., Jr., 37 E. Orange St., Lancaster, Pa.
1914. Austin, J. Harold, 821 Maloney Clinic, Univ. of Pa.
1935. Bach, Theodore F., 1900 Rittenhouse Sq.
1942. Bachman, Carl, Univ. of Pa. Hospital.
1937. Bacon, Emily P.,1930 Chestnut St.
1946. Baker, Walter W., 255 S. 17th St.
1916. Balentine, Percy L., 407 Weightman Bldg., 1524 Chestnut St.
1898. Balliet, Tilghman M., 3920 Sansom St.
1940. Barba, Philip S., 222 W. Harvey St.
1943. Barden, Robert P., 3400 Spruce St.
1911. Barnard, Everett P., 1820 S. Rittenhouse Sq.
1939. Barnshaw, Harold D., 406 Cooper St., Camden, N. J.
1939. Bartle, Harvey Jr., 133 S. 36th St.
1924. Bartle, Henry J., 1930 Chestnut St.
1931. Bates, William, 2029 Pine St.
1932. Batson, Oscar V., 3502 Hamilton St.
1921. Bauer, Edward L., 1609 Spruce St.
1933. Bauer, John T., 312 E. Second St., Moorestown, N. J.
1939. Baumann, Frieda, 1930 Chestnut St.
1922. Bazett, Henry C., Medical School, Univ. of Pa.
1908. Beardsley, E. J. G., 1919 Spruce St.
1930. Beardwood, Joseph T., Jr., 2031 Locust St.
1935. Beerman, Herman, 2422 Pine St.
1932. Behney, Charles A., 3722 Chestnut St.
1942. Behrend, Albert, 255 S. 17th St.
1945. Behrend, Bernard, 5910 Greene St.
1934. Behrend, Moses, 255 S. 17th St.
1930. Belk, William Parks, Times Medical Bldg., Ardmore, Pa.

1936. Bell, Benjamin Tertius, Abington Memorial Hospital, Abington, Pa.
1947. Bellet, Samuel, 2021 Spruce St.
1943. Berk, J. Edward, Medical Tower Bldg.
1941. Bernstein, Mitchell, 1321 Spruce St.
1937. Bertolet, J. Allen, 1530 Locust St.
1934. Biddle, Sydney Geoffrey, 255 S. 17th St.
1918. Billings, Arthur E., 2020 Spruce St.
1917. Birdsall, Joseph C., 139 Booth Lane, Haverford, Pa.
1933. Bishop, Paul A., Pennsylvania Hospital.
1944. Blady, John V., 222 Meeting House La., Merion, Pa.
1917. Block, Frank B., 136 S. 16th St.
1929. Bockus, Henry L., 250 S. 18th St.
1928. Boles, Russell S., Rittenhouse Plaza.
1923. Bond, Earl D., 111 N. 49th St.
1911. Bonney, Charles W., 255 S. 17th St.
1931. Bortz, Edward Le Roy, 2021 W. Girard Ave.
1921. Borzell, Francis Frank, 4940 Penn St.
1936. Bostwick, Delazon Swift, 106 Linwood Ave., Ardmore, Pa.
1928. Bothe, Albert E., 255 S. 17th St.
1928. Bothe, Frederick A., 255 S. 17th St.
1947. Bourland, Henry S., 2029 Delancey St.
1923. Bower, John O., 2008 Walnut St.
1942. Bowie, Morris A., 910 Old Lancaster Road, Bryn Mawr, Pa.
1907. Boyer, Henry P., 4602 Baltimore Ave.
1925. Boykin, Irvine M., 136 S. 16th St.
1907. Bradley, William Nathaniel, 1725 Pine St.
1942. Branen, William, Whitby & Cypress Ave., Yeadon, Pa.
1921. Bransfield, John W., 2101 Spruce St.
1946. Brisco, Clarence Conway, Medical Tower, 255 S. 17th St.
1917. Bromer, Ralph S., 318 Milbank Road, Bryn Mawr, Pa.
1936. Brown, Charles L., 1030 Indian Creek Rd.
1936. Brown, Clark E., Lankenau Hospital.
1932. Brown, Claude P., 1930 Chestnut St.
1939. Brust, Raymond W., 4710 Chester Ave.
1930. Bucher, Carl Joseph, The Westbury, 15th & Spruce Sts.
1943. Buerki, Robin C., University of Pa.
1928. Burden, Verne G., 255 S. 17th St.
1940. Burnett, W. Emory, 3401 N. Broad St.
1941. Butler, Miriam, 1930 Chestnut St.
1906. Butler, Ralph, 1930 Chestnut St.
1907. Cadwalader, Williams B., 133 S. 36th St.
1928. Campbell, Edward H., Spruce Street Medical Bldg., 19th & Spruce Sts.
1944. Campion, Richard J., Penllyn Rd., Springhouse, Ambler, Pa.
1931. Cantarow, Abraham, 1025 Walnut St.
1935. Carey, Lawrence S., 1930 Chestnut St.
1931. Cariss, Walter L., 2043 Walnut St.
1930. Carpenter, Chapin, 1930 Chestnut St.
1905. Carpenter, Herbert B., 1805 Spruce St.
1926. Carpenter, Howard Childs, 1805 Spruce St.
1917. Carson, John B., 1802 Pine St.
1922. Case, Eugene A., 63 W. La Crosse Ave., Landsdowne, Pa.
1937. Castallo, Mario A., 1621 Spruce St.
1943. Castigliano, S. Gordon, 1012 Hampstead Rd., Penfield Downs, Del. Co., Pa.

1933. Chamberlain, W. Edward, Temple University Hospital.
1939. Chamberlain, George W., Reading Hospital, Reading, Pa.
1900. Chance, Burton, 317 S. 15th St.
1945. Chance, Burton, Jr., 1726 Spruce St.
1939. Charr, Robert Kyun Hyun, 2038 Locust St.
1941. Cheleden, John, 255 S. 17th St.
1947. Chouké, Kehar S., 4111 Walnut St.
1945. Cianfrani, Theodore, 1930 Chestnut St.
1939. Ciccone, Emmet F., 2021 Murray St.
1929. Clark, Eliot R., 315 S. 41st St.
1934. Clark, Jefferson Hamer, 3701 N. Broad St.
1947. Clark, Thomas Williams, 400 E. Willow Grove Ave.
1947. Classen, Charles H., Cushman Rd. and Lancaster Ave.
1926. Clerf, Louis H., 1530 Locust St.
1910. Cloud, J. Howard, 111 St. Pauls Road, Ardmore, Pa.
1903. Coates, George Morrison, 1721 Pine St.
1908. Codman, Charles A. E., S.E. Corner 42d and Spruce Sts.
1941. Cohen, J. Gershon, 255 S. 17th St.
1907. Cohen, Myer Solis-, 2110 Spruce St.
1888. Cohen, S. Solis-, Mountain & Cheltenham Aves.
1920. Cole, Charles J., 7926 Park Ave., Elkins Park, Pa.
1934. Colgan, Robert C., Bridgeport, Pa.
1934. Collins, Leon Howard, Jr., 133 S. 36th St.
1943. Colonna, Paul C., Univ. of Pa. Hospital.
1945. Coonel, Pauline, 47 E. Mt. Pleasant Ave.
1930. Cooper, David A., 1520 Spruce St.
1947. Coppolino, John F., 1807 S. Broad St.
1941. Cornelius, Chalmers E., 119 Summit Ave., Jenkintown, Pa.
1911. Cornell, Walter S., Board of Public Education, Parkway and 21st St.
1945. Corrigan, Patrick H., 1720 S. Broad St., Trenton, N. J.
1914. Corson, Edward F., 136 S. 16th St.
1946. Costello, Thomas J., 131 Pennsylvania Avenue, Bryn Mawr, Pa.
1924. Cowan, Alfred, 1930 Chestnut St.
1940. Cowan, Thomas H., 1930 Chestnut St.
1904. Craig, Frank A., The Henry Phipps Institute, 7th and Lombard Sts.
1907. Crampton, George S., 2031 Locust St.
1947. Crane, A. Reynolds, 807 Spruce St.
1937. Crane, Martin P., 2412 N. Broad St.
1920. Creighton, William J., 37 S. 20th St.
1941. Creskoff, Adolph J., 3400 Spruce St.
1920. Cross, George H., Chester, Pa.
1917. Cross, Sumner H., P. O. Box 126, Jenkintown, Pa.
1921. Crossan, Edward T., 5324 Wayne Ave.
1940. Crowe, Aldrich C., 735 Atlantic Ave., Ocean City, N. J.
1904. Cruice, John M., 407 S. 22d St.
1937. Crump, Jean, 1930 Chestnut St.
1937. Curtis, Lawrence, 255 S. 17th St.
1934. Custer, R. Philip, 221 Walnut Ave., Wayne, Pa.
1941. *Cuttle, Tracy D.
1947. Cutler, Norman L., 1300 Harrison St.
1938. Dannenberg, Arthur M., 235 S. 15th St.

*On active service.

LIBRARY OF THE
COLLEGE OF PHYSICIANS
OF PHILADELPHIA

1919. Davies, John R., Jr., 2 E. Chestnut Ave., Chestnut Hill.
1947. Davis, C. Nelson, 133 South 36th St.
1936. Davis, David M., 255 S. 17th St.
1937. Davis, Perk Lee, 255 S. 17th St.
1935. Deaver, J. Montgomery, 1830 Delancey Pl.
1947. Deihne, Theodore L., Adams Avenue and Roosevelt Blvd.
1902. Dehoney, Howard, 240 S. 13th St.
1935. Deibert, Irvin Elmer, 538 Cooper St., Camden, N. J.
1924. Deichler, L. Waller, 1930 Chestnut St.
1923. De Long, Perce, 37 S. 20th St.
1928. Dewees, A. Lovett, Times Medical Bldg., Ardmore, Pa.
1924. Dillon, Edward S., 2016 Delancey Pl.
1932. Dintenfass, Henry, 1305 Spruce St.
1920. Diven, John, 1827 Delancey St.
1920. Doane, Joseph C., 617 W. Hortter St.
1946. Donnelly, Andrew J., 4931 State Road, Drexel Hill, Pa.
1942. Donnelly, Edward J., 1321 Spruce St.
1933. Donnelly, Joseph C., 255 S. 17th St.
1937. Donnelly, Robert T. M., 255 S. 17th St.
1907. Dorrance, George M., 2101 Spruce St.
1910. Drayton, William, Jr., 1930 Spruce St.
1935. Duane, William, Jr., 2100 Walnut St.
1944. Dublin, George J., 1930 Chestnut St.
1944. Dugger, John H., 3902 Vaux St.
1935. Duncan, Garfield G., 330 S. 9th St.
1937. Dunn, Charles W., 269 S. 19th St.
1942. Durant, Thomas M., 3401 N. Broad St.
1947. Durkin, John Kennan, 34 W. Montgomery Ave.
1942. Dyer, W. Wallace, Univ. of Pa. Hospital.
1935. Eads, John T., 2029 Delancey St.
1911. Earnshaw, Henry C., Bryn Mawr, Pa.
1936. Easby, Mary Hoskins, 1930 Chestnut St.
1937. Edeiken, Joseph, 2130 Delancey Pl.
1944. Eger, Sherman A., 2029 Delancey St.
1944. Ehrich, William E., 236 W. Hortter St.
1930. Eiman, John, Cynwyd, Pa.
1946. Elfman, Louis Kenneth, 6330 Lebanon Avenue.
1911. Eliason, Eldridge L., 326 S. 19th St.
1939. Ellis, Van Mashburn, 1530 Locust St.
1928. Ellison, Richard T., 269 S. 19th St.
1936. Ellson, J. Vernon, Glendale Rd. & Chestnut St., Upper Darby, Pa.
1904. Elmer, Walter G., 1801 Pine St.
1937. Elsom, Kendall A., 133 S. 36th St.
1934. Ely, William C., 3912 Chestnut St.
1932. Engel, Gilson G., 255 S. 17th St.
1945. English, O. Spurgeon, 255 S. 17th St.
1942. Erb, William H., 133 S. 36th St.
1893. Eshner, Augustus A., 1019 Spruce St.
1944. Estes, William L., Jr., Bethlehem, Pa.
1946. Farell, David M., 1831 Delancey St.
1922. Farley, David L., 4429 Larchwood Ave.
1903. Farr, Clifford B., Bryn Mawr, Pa.
1945. Farrar, George Elbert, Jr., 425 Tregaron Rd., Bala-Cynwyd, Pa.

1947. Farrell, Harry L., 1930 Chestnut St.
1930. Farrell, John T., Jr., 255 S. 17th St.
1935. Ferguson, Lewis Kraeer, 133 S. 36th St.
1936. Fetter, Ferdinand, 322 S. 21st St.
1945. Fetter, John S., 1010 Rhawn St.
1935. Fetter, Theodore R., 255 S. 17th St.
1924. Fewell, Alexander G., 1924 Pine St.
1943. Finkelstein, Arthur, 645 Overhill Rd., Ardmore, Pa.
1947. First, Arthur, 1714 Spruce St.
1945. Fiske, Frederick A., 1530 Locust St.
1928. Fitz-Hugh, Thomas, Jr., 2016 Delancey Pl.
1928. Flick, John B., 330 S. 9th St.
1939. Flippin, Harrison F., 255 S. 17th St.
1946. Forster, Francis M., Jefferson Medical College.
1941. Fox, C. Calvin, 1806 Spruce St.
1906. Fraley, Frederick, 71st and City Line, Overbrook, Pa.
1941. Frazier, William Doane, 133 S. 36th St.
1935. Fridy, Cyrus Ward, P.O. Box 28, Collegeville, Pa.
1942. Friedman, Reuben, 877 N. 6th St.
1933. Fritch, James Scott, 269 S. 19th St.
1937. Fritz, Herbert H., Pennswood Rd., Bryn Mawr, Pa.
1940. Fry, Kenneth E., 255 S. 17th St.
1935. Fry, Wilfred Eyles, 1819 Chestnut St.
1937. Furlong, Thomas F., Jr., Times Medical Building, Armore, Pa.
1935. Gammon, Geo. D., Univ. of Pa. Hospital.
1931. Garner, Vaughn C., Germantown Professional Building.
1947. Gaskill, Herbert Stockton, 39 Summit St.
1935. Geist, Donald C., 5302 Spruce St.
1917. Gerhard, Arthur H., 1615 N. Delaware Ave.
1899. Gibbon, John H., Media, Pa.
1934. Gibbon, John H., Jr., 1025 Walnut St.
1939. Gibson, Glen Gregory, 255 S. 17th St.
1944. Gifford, Edward S., Jr., 1913 Spruce St.
1933. Gifford, U. Grant, Kennett Square, Pa.
1920. Gill, A. Bruce, 1930 Chestnut St.
1927. Gilmour, William R., 413–14 Weightman Bldg., 1524 Chestnut St.
1931. Giordano, Anthony A. S., 1819 S. Broad St.
1906. Gittings, John C., Harwood, Md.
1906. Goepp, R. Max, 1333 Chestnut St.
1945. Goldberg, Samuel J., 1723 Pine St.
1933. Goldburgh, Harold L., 1932 Spruce St.
1935. Goldsmith, N. Ralph, 136 S. 16th St.
1905. Gordon, Alfred, 1520 Spruce St.
1928. Gordon, Burgess L., 1832 Spruce St.
1937. Gordon, William, ~~1721 Pine St.~~ 5345 Spruce St. Phila 34.
1941. Gouterman, Joseph I., 1930 Chestnut St.
1947. Grady, Hugh G., Jefferson Medical College.
1894. Graham, Edwin E., 1713 Spruce St.
1926. Grant, Francis Clark, Univ. of Pa. Hospital.
1933. Greenbaum, Sigmund S., 320 S. 18th St.
1940. Greene, Lloyd B., 136 S. 16th St.
1934. Griffith, John Q., Jr., 133 S. 36th St.
1945. Griffiths, John E., Mermont Apartments, Bryn Mawr, Pa.

1941. Groff, Robert A., 700 Univ. of Pa. Hospital.
1933. Gruber, Charles M., 128 Overhill Rd., Cynwyd, Pa.
1932. Guequierre, Jacques P., Mermont Plaza, Bryn Mawr, Pa.
1944. Gunter, John H., 1306 Knox Rd., Wynnewood, Pa.
1945. György, Paul, Univ. of Pa.
1935. Hadden, Samuel B., 37 S. 20th St.
1945. Hahn, George A., 255 S. 17th St.
1935. Haines, Harlan F., 134 S. State Rd., Upper Darby, Pa.
1939. Hamblock, Leonard C., 255 So. 17th St.
1894. Hamill, S. McC., 1822 Spruce St.
1897. Hand, Alfred, 1724 Pine St.
1938. Hand, John G., 1724 Pine St.
1947. Hanes, William James, Berkley Road, Devon, Pa.
1932. Harris, Stanley E., Lansdowne, Pa.
1929. Harrison, Francis G., 1900 Spruce St.
1933. Harrison, William John, 135 S. 17th St.
1903. Hart, Charles D., 420 W. Mermaid Lane.
1941. Hartley, Harriet L., 1719 Rittenhouse Square.
1932. Hartman, J. Calvin, 50 W. Walnut Lane.
1926. Hartmann, Fred L., 1914 Pine St.
1946. Harvey, Edith E., 1930 Chestnut St.
1947. Harvey, Rolfe Marsh, Bryn Mawr Hospital.
1935. Haskell, Benjamin F., 1426 Spruce St.
1946. Hatfield, C. Alexander, 2019 Spruce St.
1907. Hatfield, Charles James, Henry Phipps Institute, 7th and Lombard Sts.
1947. Havens, Walter Paul, Jr., 300 Cherry Lane, Wynnewood, Pa.
1947. Hawthorne, Herbert Reid, 606 North 13th St.
1911. Heed, Charles R., 1205 Spruce St.
1946. Hendrickson, Frank O., 37 S. 20th St.
1944. Herbut, Peter A., Jefferson Medical College Hospital.
1927. Herman, Leon, 136 S. 16th St.
1944. Hershey, J. Ivan, 935 Bowman Ave., Wynnewood, Pa.
1924. Hewson, William, 2031 Locust St.
1924. Hirst, John C., 2d, 500 N. 20th St.
1944. Hirst, Otto C., 255 S. 17th St.
1908. Hitchens, Arthur Parker, Dept. Public Health, Wilmington, Del.
1943. Hitschler, William J., 8840 Germantown Ave.
1944. Hneleski, Ignatius S., 802 S. 48th St.
1943. Hockaday, Agnes, 316 Shadeland Ave., Drexel Hill, Pa.
1939. Hodes, Philip J., Univ. of Pa. Hospital.
1947. Hodges, John H., 1025 Walnut St.
1931. Holland, H. Albert, 8200 Crittenden St., Chestnut Hill.
1932. Hollingsworth, I. Pemberton P., 411 N. Walnut St., West Chester, Pa.
1919. Hopkins, Arthur H., 1726 Pine St.
1925. Hopkinson, R. Dale, Jenkintown, Pa.
1946. Horan, Gerald W., 5819 Chester Ave.
1947. Horwitz, Orville, 237 W. Montgomery Ave., Haverford, Pa.
1944. Housel, Edmund L., 255 S. 17th St.
1928. Houser, Karl Musser, 2010 Spruce St.
1938. Howell, John Carnett, 326 S. 19th St.
1946. Howson, John Yeatts, 3722 Chestnut St.
1947. Huber, John Franklin, Temple University Hospital.
1937. Hughes, Joseph, 111 N. 49th St.

1939. Hughes, P. Boland, 419 Hillbrook Rd., Bryn Mawr, Pa.
1923. Hume, John E., 37 S. 20th St.
1946. Hunt, William T., Jr., 1205 Spruce St.
1921. Hunter, Robert John, 2035 Delancey Pl.
1926. Husik, David N., 1820 Spruce St.
1935. Ingleby, Helen, Jewish Hospital, York & Tabor Rds.
1947. Israel, S. Leon, 2116 Spruce St.
1921. Ivy, Robert H., 1930 Chestnut St.
1917. Jackson, Chevalier, 255 S. 17th St.
1932. Jackson, Chevalier L., 255 S. 17th St.
1934. Jacobs, Maurice, 1831 Delancey Place.
1947. Jaeger, Rudolph, Jefferson Hospital.
1941. Jeffers, William A., University of Pa. Hospital.
1928. John, Rutherford L., 256 S. 21 St.
1942. Johnson, Julian, 406 Conshohocken State Rd., Narberth, Pa.
1938. Johnson, Thomas A., 250 S. 18th St.
1918. Jonas, Leon, 255 S. 17th St.
1943. *Jones, Charles Alexander.
1924. Jones, Harold W., 1930 Chestnut St.
1900. Judson, Charles F., 252 Kent Road, Wynnewood, Pa.
1936. Kain, Thomas M., 403 Cooper St., Camden, N. J.
1938. Kasper, Kelvin A., 135 S. 18th St.
1945. Katz, G. Henry, 111 N. 49th St.
1941. Kauffman, M. Luther, Medical Arts Bldg., Jenkintown, Pa.
1947. Kay, Calvin Frederick, Univ. of Pa. Hospital.
1947. Keefer, George Pfahler, 1930 Chestnut St.
1938. Keeler, Harold R., 136 S. 16th St.
1935. Kelley, George F. J., N.E. Cor. 20th and Chestnut Sts.
1932. Kelly, Herbert T., 1900 Spruce St.
1912. Kelly, Thomas C., 105 School Lane.
1941. Kennedy, Patrick J., 6910 Market St., Upper Darby, Pa.
1947. Kennedy, William Blair, 3400 Spruce St.
1921. Kern, Richard A., University of Pa. Hospital.
1935. Keyes, Baldwin L., 2031 Locust St.
1930. Kimbrough, Robert A., Jr., 807 Spruce St.
1936. King, Orville C., 330 S. 9th St.
1920. Klauder, Joseph V., 1934 Spruce St.
1920. Klein, Thomas, 250 S. 18th St.
1934. Kline, Oram R., 414 Cooper St., Camden, N. J.
1932. Klopp, John W., 600 W. Olney Ave.
1943. Kneedler, William H., 8801 Crefeld St.
1919. Knipe, Norman L., 1930 Chestnut St.
1908. Knowles, Frank C., 2035 Spruce St.
1938. Knox, Andrew, 1930 Chestnut St.
1925. Knox, Harry E., 719 66th Ave.
1945. Kobler, H. B., 658 N. 63rd St.
1914. Kolmer, John A., Cynwyd, Pa.
1936. Konzelmann, Frank Williamson, 304 Shore Rd., Absecon, N. J.
1941. Krall, J. Thomas, 1927 Spruce St.
1944. Krauss, Frederick Harold, 1930 Chestnut St.
1941. Krewson, William E., 3rd, 1930 Chestnut St.

* On active service.

1914. Krumbhaar, Edward B., School of Medicine, Univ. of Pa.
1947. Kuhlenbeck, Hartwig, Woman's Medical College.
1947. La Boccetta, Alfred Charles, 2nd and Luzerne Sts.
1944. LaMotte, William O., Medical Arts Bldg., Wilmington, Del.
1946. Lampe, William T., 4207 Tyson Ave.
1907. Langdon, H. Maxwell, 1530 Locust St.
1933. Langdon, Roy L., 5917 Greene St., Germantown.
1941. Langner, Paul H., Jr., 130 S. 18th St.
1945. Lansbury, John, 3401 N. Broad St.
1934. Laplace, Louis B., 1520 Spruce St.
1926. Laws, George M., 1907 Spruce St.
1936. Leaman, William G., Jr., 3700 Baring St.
1920. Leavitt, Frederic Headley, 1527 Pine St.
1941. Leberman, Paul R., 136 S. 16th St.
1934. Lee, Thomas B., 622 Cooper St., Camden, N. J.
1908. Lee, Walter Estell, 1833 Pine St.
1942. Lehman, James A., 255 S. 17th St.
1936. Lehrfeld, Louis, 1321 Spruce St.
1944. Lell, William A., 203 W. Chestnut Ave.
1935. Lemmon, William T., 1930 Chestnut St.
1943. Leopold, Irving H., 1930 Chestnut St.
1920. Leopold, Simon S., 2025 Spruce St.
1944. Lettiere, Anthony J., 425 E. State St., Trenton, N. J.
1933. Levering, J. Walter, Abington Memorial Hospital, Abington, Pa.
1915. Lewis, Fielding O., Providence Road, Media, Pa.
1938. Lewis, James P., 3815 Chestnut St.
1940. Limberger, William A., 301 S. Church St., West Chester, Pa.
1938. Lindauer, M. August, 133 S. 36th St.
1927. Lindsey, Walter H., 810 W. Dauphin St.
1936. Lintgen, Charles, 1930 Chestnut St.
1945. Lisker, Samuel, 1930 Chestnut St.
1944. Livezey, Mary M., 7200 Cresheim Rd.
1936. Llewellyn, Thomas H., 910 N. 63rd St.
1907. Lodholz, Edward, 431 S. 45th St.
1931. Loewenberg, Samuel A., 1905 Spruce St.
1938. Long, Charles-Francis, 1836 Delancey Pl.
1933. Long, Esmond R., Henry Phipps Institute, 7th and Lombard Sts.
1935. Long, William L., 2025 Walnut St.
1893. Longaker, Daniel, 5702 Overbrook Ave.
1931. Longaker, Edwin P., 41 E. Montgomery Ave., Ardmore, Pa.
1944. Loudenslager, Paul E., 2101 Spruce St.
1942. Lownes, John B., 136 S. 16th St.
1936. Lucchesi, Pascal Francis, Philadelphia General Hospital.
1921. Lucké, Balduin H. E., School of Medicine, Univ. of Pa.
1932. Lukens, Francis D. W., Univ. of Pa. Hospital.
1938. Lukens, Philip Jefferson, 158 E. Butler Ave., Ambler, Pa.
1930. Lukens, Robert M., Medical Arts Bldg., 16th and Walnut Sts.
1929. Lull, Clifford B., Women's Bldg., Penna. Hosp., 807 Spruce St.
1939. Luongo, Romeo A., 2054 Locust St.
1947. Lurie, Max B., Henry Phipps Institute.
1919. Lynch, Frank B., Jr., Germantown Hosp., Penn and Chew Sts.
1914. Lyon, B. B. Vincent, Box 955, Winter Park, Fla.
1933. McAndrews, Leo F., Mermont Plaza, Bryn Mawr, Pa.

1932. McCahey, James F., 1534 Pine St.
1900. McCarthy, Daniel J., 2025 Walnut St.
1936. McCarthy, Patrick A., Central Medical Bldg.
1935. McClenahan, William U., 5 E. Chestnut Ave.
1931. McCloskey, Edward, 7 E. Chestnut Ave.
1942. McCloskey, John F., 8720 Germantown Ave.
1935. McConnell, James W., 20th and Chestnut Sts.
1934. McCouch, Grayson P., Medical School, Univ. of Pa.
1938. McCrea, Lowrain E., 1930 Chestnut St.
1937. McCutcheon, Morton, Alden Park Manor.
1942. McDonald, P. Robb, 255 S. 17th St.
1945. McGee, Lemuel Clyde, Hercules Powder Company, Wilmington, Del.
1937. McGuinness, Aims C., 8614 Montgomery Ave.
1940. McLaughlin, Edward F., 4116 N. Broad St.
1933. McLaughlin, James S., 330 S. 9th St.
1924. McMillan, Thomas M., 2044 Locust St.
1924. McPhedran, F. Maurice, Germantown Hosp., Penn and Chew Sts.
1943. Macfarlan, Douglas, 1805 Chestnut St.
1932. Macfarlane, Catharine, 136 S. 16 St.
1947. Machella, Thomas E., 232 S. 39th St.
1939. Macneill, Norman N., 5807 Chew St.
1935. Maeder, LeRoy M. A., 204 S. 13th St.
1935. Maier, Ernest G., 1323 N. 15th St.
1942. Manges, Lewis C., Jr., 319 S. 16th St.
1936. Mann, Bernard, 2019 Pine St.
1937. Margolies, Alexander, 255 S. 17th St.
1941. Martin, James R., 136 S. 16 St.
1935. Matthews, Robert A., 111 N. 49th St.
1939. May, Hans, 255 S. 17th St.
1934. Mecray, Paul M., 405 Cooper St., Camden, N. J.
1914. Mencke, J. Bernhard, 1816 Spruce St.
1941. Mendell, Theodore H., 2023 Spruce St.
1943. Meranze, David R., 1031 Lakeside Ave.
1937. Meyer, George Phillip, 410 Haddon Ave., Camden, N. J.
1935. Miller, Ford A., 4016 Chestnut St.
1946. Miller, Franklin R., Jefferson Medical College.
1934. Miller, Hugh McCauley, 1614 Locust St.
1939. Miller, Malcolm W., 255 S. 17th St.
1939. Miller, Merle M., 6013 Greene St.
1932. Miller, M. Valentine, 114 W. Phil-Ellena St.
1921. Miller, T. Grier, 133 So. 36th St.
1937. Missett, Joseph Vincent, Jr., 2031 Locust St.
1904. Mitchell, Charles Franklin, 2003 Pine St.
1932. Mohler, Roy W., 1806 Spruce St.
1936. Montgomery, Hugh, 119 Glenn Road, Ardmore, Pa.
1936. Montgomery, John B., 1930 Chestnut St.
1932. Montgomery, Thaddeus L., 2031 Locust St.
1928. Moon, Virgil H., Jefferson Medical College.
1935. Moore, John Royal, Beury Bldg., Broad St. and Erie Ave.
1947. Moore, Matthew Thibaud, 1913 Delancey Pl.
1924. Moorhead, Stirling W., 1523 Pine St.
1936. Morgan, David R., Jefferson Medical College.
1893. Morris, Elliston J., 439 Midland Ave., St. Davids, Del. Co., Pa.

1944. Morris, Harold H., Villa Nova, Pa.
1945. Morris, I. Paul, 255 S. 17th St.
1941. Mucklé, Craig Wright, 255 S. 17th St.
1929. Mudd, Stuart, Department of Bacteriology, Medical School, Univ. of Pa.
1935. Mullen, Carroll Richard, 2025 Locust St.
1934. Mullen, Edward A., 6445 Greene St.
1930. Murphy, Douglas P., Univ. of Pa. Hospital.
1934. Murphy, Eugene C., 1841 S. Broad St.
1905. Mutschler, Louis H., 1625 Spruce St.
1945. Naide, Meyer, 2034 Spruce St.
1936. Nelson, Guy M., 255 S. 17th St.
1943. Nelson, Waldo E., 615 Moreno Rd., Narberth, Pa.
1905. Newcomet, William S., 3501 Baring St.
1938. Newton, Zachariah B., 601 E. Sedgwick St.
1935. Nicholson, Jesse Thompson, Pennsylvania Hospital.
1899. Nicholson, William Rufus, 1930 Chestnut St.
1941. Nisbet, Verner, 254 S. 45th St.
1947. Noone, Ernest L., 4501 Cedar Lane, Drexel Hill, Pa.
1905. Norris, Charles C., Darby and Goshen Roads, Bryn Mawr, Pa.
1938. Norris, Robert F., 513 Wynnewood Ave., Wynnewood, Pa.
1947. Oaks, Wilbur W., 606 North 13th St.
1941. Odenatt, Wm. Burrill, 1213 W. Lehigh Ave.
1947. O'Keefe, John J., 255 South 17th St.
1913. O'Neal, Alexander Hay, St. Davids, Pa.
1947. Ornsteen, A. M., 2007 Delancey Pl.
1947. Ornston, Darius Gray, 36 Carpenter Lane.
1936. Orr, Theodore E., 1930 Chestnut St.
1913. Outerbridge, George W., 1927 Spruce St.
1915. Owen, Hubley R., Board of Education, 21st & Parkway.
1897. Packard, Francis R., 304 S. 19th St.
1909. Parish, Benjamin Dores, 1927 Spruce St.
1945. Park, Felix Roman, Medical Arts Bldg., Tulsa, Okla.
1940. Parker, Alan P., 330 S. 9th St.
1944. Paschkis, Karl E., Jefferson Medical College.
1931. Paul, John Davis, 3112 N. Broad St.
1932. Payne, Franklin L., Univ. of Pa. Hospital.
1947. Pearce, Louise, Rockfeller Institute for Medical Research, Princeton, N. J.
1943. Pearson, Gerald H., 111 N. 49th St.
1909. Pemberton, Ralph, Paoli, Pa.
1930. Pendergrass, Eugene P., Univ. of Pa. Hospital.
1932. Pennell, Howard Y., West Chester, Pa.
1944. Pennypacker, Charles S., 111 E. Montgomery Ave., Ardmore, Pa.
1939. Pepper, D. Sergeant, 122 Grays Lane, Haverford, Pa.
1914. Pepper, O. H. Perry, Univ. of Pa. Hospital.
1916. Percival, Milton Fraser, 2332 S. Broad St.
1942. Perkins, William Harvey, 1025 Walnut St.
1946. Perloff, William Harry, 2106 Spruce St.
1940. Pessel, Johannes F., 224 West State St., Trenton, N. J.
1937. Pettit, Horace, P.O. Box 96, Gladwyne, Pa.
1905. Pfahler, George E., 1930 Chestnut St.
1915. Pfeiffer, Damon B., Meadowbrook, Pa.
1946. Pfeiffer, Mildred C. J., 331 S. Smedley St.
1935. Phillips, Arthur W., 3904 Walnut St.

1911. Piersol, George Morris, Univ. of Pa. Hospital.
1933. Pillsbury, Donald M., 133 S. 36th St.
1922. Pleasants, Henry, Jr., West Chester, Pa.
1937. Polk, David Stewart, Rosemont, Pa.
1932. Porter, Roland De Lance, Jenkintown, Pa.
1947. Prickett, John A., Warrington, Bucks County, Pa.
1931. Pryor, Charles Allen, 255 S. 17th St.
1947. Putney, Floyd Johnson, 255 South 17th St.
1943. Radbill, Samuel X., 7043 Elmwood Ave.
1945. Rakoff, Abraham Edward, 2001 Delancey Pl.
1931. Ramsey, Frank M., Chestnut Hill.
1913. Randall, Alexander, 136 S. 16 Street.
1941. Rankin, Charles A., Ludlow & Heather Rd., Upper Darby, Pa.
1946. Rapoport, Milton, Children's Hospital, 1740 Bainbridge St.
1926. Ravdin, I. S., Univ. of Pa. Hospital.
1938. Read, Hilton Shreve, 5407 Atlantic Ave., Atlantic City, N. J.
1928. Reese, Warren S., 1901 Walnut St.
1925. Reeves, Rufus S., 2227 Spruce St.
1920. Rehfuss, Martin E., 131 St. George's Rd., Ardmore, Pa.
1921. Reiff, E. Paul, 1927 Spruce St.
1937. Reimann, Hobert A., Jefferson Hospital.
1919. Reimann, Stanley P., 703 W. Phil-Ellena St.
1923. Repplier, Sidney J., 373 Roumfort Rd., Mt. Airy.
1945. Rhoads, Jonathan E., Univ. of Pa. Hospital.
1936. Richards, James L., Haverford Villa, Ardmore, Pa.
1919. Richardson, Russell, 320 S. 16th St.
1919. Ridpath, Robert F., 1737 Chestnut St.
1942. Riggs, Helena E., Philadelphia General Hospital.
1936. Ritter, Joseph A., 2405 N. 54th St.
1933. de Rivas, Damaso, 1831 Chestnut St.
1942. Rivers, Thurston D., 111 N. 49th St.
1932. Robbins, Frederick R., 317 Millbank Rd., Bryn Mawr, Pa.
1939. Roberts, Ella, 133 S. 36th St.
1944. Roberts, Joseph E., 403 Cooper St., Camden, N. J.
1899. Roberts, Walter, 1921 Spruce St.
1932. Robertson, Harold F., 327 S. 17th St.
1903. Robertson, William Egbert, 327 S. 17th St.
1938. Roche, Philip Q., 255 S. 17th St.
1912. Rodman, John Stewart, 1726 Spruce St.
1947. Rogers, Arthur Merriam, 133 S. 36th. St.
1934. Rogers, Harry L., Riverton, N. J.
1928. Rose, Edward, 426 Owen Rd., Wynnewood, Pa.
1936. Rose, Elizabeth Kirk, 426 Owen Rd., Wynnewood, Pa.
1946. Rosemond, George Parrott, Temple University, Broad & Ontario Sts.
1932. Rothrock, Harry A., West Chester, Pa.
1936. Rothschild, Norman, 245 S. 16th St.
1933. Rowntree, Leonard George, 1520 Spruce St.
1937. Roxby, John B., P.O. Box #28, Swathmore, Pa.
1941. Royster, Hubert A., Jr., The Mermont, Bryn Mawr, Pa.
1933. Rudolphy, Jay Besson, 230 S. 21st St.
1946. Rupp, Charles, 2315 Delancey Pl.
1947. Rush, Alexander, 330 South 9th St.
1945. Rynes, Samuel E., 334 S. 21st St.

1944. Sampson, David Alan, 726 Braeburn Lane, Penn Valley, Narberth, Pa.
1936. Sands, Joseph Evans, Rosemont, Pa.
1908. Sautter, Albert C., Germontown Professional Bldg.
1947. Sayen, John J., 376 Montgomery Pike, Wynnewood, Pa.
1920. Scarlett, Hunter W., 825 Montgomery Ave., Bryn Mawr, Pa.
1939. Scattergood, Joseph Jr., 115 S. High St., West Chester, Pa.
1917. Schaeffer, J. Parsons, Daniel Baugh Institute, 307 S. 11th St.
1929. Scheffey, Lewis C., 255 S. 17th St.
1942. Scheie, Harold G., 313 S. 17th St.
1929. Schenck, Harry P., 1235 Wyngate Rd., Wynnewood, Pa.
1945. Schlezinger, Nathan S., Medical Tower Building.
1917. Schnabel, Truman G., 1704 Pine St.
1917. Schoff, Charles H. Media, Pa.
1928. Schofield, Frederick S., 5501 Greene St.
1921. Schumann, Edward A., 1814 Spruce St.
1930. Scott, John Porter, 1740 Bainbridge St.
1940. Scott, T. F. McNair, Children's Hospital, 1740 Bainbridge St.
1924. Shallow, Thomas A., 1611 Spruce St.
1908. Shannon, Charles E. G., 1930 Chestnut St.
1928. Sharpless, Frederick C., Rosemont, Pa.
1931. Sheehan, William C., 8811 Germantown, Ave.
1946. Shepherd, Samuel Garfield, 2039 Pine St.
1932. Sheridan, Joyce T., 412 W. Durham St.
1943. Shewbrooks, Daniel M., Penn Mutual Life Ins. Co., 6th and Walnut Sts.
1936. Shipman, James Shelby, 255 S. 17th St.
1935. Shoemaker, Robert, 3rd., 68 Byberry Rd., Hatboro, Pa.
1946. Shoup, George Daniel, 7007 N. 12th St.
1939. Shumway, Norman P., Crile Veterans Administration Hospital, Cleveland, Ohio.
1936. Shuster, Benjamin H., 1824 Pine St.
1941. Silcox, Louis E., 255 S. 17th St.
1903. Sinclair, John F., 4103 Walnut St.
1907. Sinkler, Francis W., P.O. Box 373, Bryn Mawr, Pa.
1928. Skillern, Samuel R., 1734 Pine St.
1933. Smelzer, Donald Campbell, Germantown Hosp., Penn and Chew Sts.
1929. Smith, Austin T., 1830 Spruce St.
1947. Smith, Frederick C., 409 S. 22nd St.
1933. Smith, Lauren Howe, 111 N. 49th St.
1927. Smyth, Calvin Mason, Room 451, Methodist Hospital, Broad and Wolf Sts.
1938. Snodgrass, L. E., 2011 Chestnut St.
1941. Snyder, G. Gordon, Mermont Apts., Bryn Mawr, Pa.
1935. Sokoloff, Martin J., 255 S. 17th St.
1940. Soloff, Louis A., 2032 Pine St.
1935. Sommer, George N. J., 120 W. State St., Trenton, N. J.
1944. Sommer, George N. J., Jr., 120 W. State St. Trenton, N. J.
1928. Spaeth, Edmund B., 1930 Chestnut St.
1937. Spangler, John Luther, Devon, Pa.
1935. Spiegel, Ernest, 6807 Lawnton Ave., Oak Lane.
1929. Sponsler, Marshall B., 1737 Chestnut St.
1944. Stadie, William C., University Hospital.
1927. Starr, Isaac, 505 Cresheim Valley Rd.
1945. Stecher, H. Armin, 1510 Darby Rd., Upper Darby, Pa.
1946. Stein, Irvin, 269 South 19th St.
1947. Steiner, Charles A., Upper Darby National Bank Building.

1936. Steinfield, Edward, N.E., Cor. 18th and Chestnut Sts.
1942. Stengel, Alfred, Jr., Lancaster Ave. and Cambria Court, St. Davids, Pa.
1947. Stewart, Genevieve M., 136 South 16th St.
1914. Stewart, Thomas S., The Barclay, 18th and Rittenhouse Sq.
1941. Stewart, Winifred B., 1930 Spruce St.
1934. Stimson, Cheney M., 167 Harvey St.
1925. Stokes, John H., 4228 Spruce St.
1928. Stokes, Joseph, Jr., 1740 Bainbridge St.
1943. Stokes, S. Emlen, 129 Chester Ave., Moorestown, N. J.
1923. Strecker, Edward A., 111 N. 49th St.
1923. Stroud, William Daniel, 1011 Clinton St.
1937. Strumia, Max M., Penn Valley, Narberth, Pa.
1933. Stuckert, Harry, 248 S. 21st St.
1937. Sturgis, Margaret C., Haverford Manor, Haverford Pa.
1927. Sturgis, Samuel Booth, Haverford Manor, Haverford, Pa.
1934. Summey, Thomas J., 330 S. 9th St.
1930. Sunderman, F. William, 2210 Delancey Pl.
1936. Surver, James Miller, 1020 Clinton St.
1928. Swartley, William B., 6002 Greene St.
1934. Sweeney, John A., 1900 Rittenhouse Sq.
1944. Swenson, Paul C., Jefferson Hospital.
1943. Tassman, Isaac S., 136 S. 16th St.
1946. Tauber, Robert, 2019 Walnut St.
1933. Taylor, Herbert W., Haverford, Pa.
1931. Taylor, Norman H., 100 W. Evergreen Ave.
1946. Thomas, Carmen C., 1930 Chestnut St.
1928. Thomas, J. Earl, Drexel Hill, Pa.
1907. Thomas, T. Turner, 1636 Francis St.
1942. Thompson, Wesley D., Jr., 18 N. Main St. Lewistown, Pa.
1927. Thorington, J. Monroe, 2031 Chestnut St.
1936. Thornton, Mary Bickings-, 2703 West Somerset St.
1936. Thorp, Francis Quicksall, 4900 Penn St.
1936. Thudium, William J., 136 S. 16th St.
1935. Tocantins, Leandro Maués, 424 W. Hortter St.
1945. Toland, Joseph J., Jr., 1241 W. Lehigh Ave.
1935. Toland, Owen J., Episcopal Hospital, Front and Lehigh Ave.
1945. Tourish, William J., Garden Court Apts.
1936. Towson, Charles Emory, Germantown Professional Bldg.
1908. Tracy, Stephen E., Beverly Hills, Upper Darby, Pa.
1947. Trueman, Robert H., 1930 Chestnut St.
1926. Tucker, Gabriel, 250 S. 18th St.
1938. Tuft, Louis, 1530 Locust St.
1933. Tumen, Henry J., 1900 Rittenhouse Sq.
1938. Turman, Christopher M., Wyncote, Pa.
1923. Turner, Creighton H., 1731 Pine St.
1945. Twyeffort, Louis H., 111 N. 49th St.
1929. Tyson, Ralph M., 255 S. 17th St.
1937. Uhle, Charles A. W., 255 S. 17th St.
1907. Ullom, Josephus T., Carpenter and Quincy Sts.
1937. Vander Veer, Joseph B., 330 S. 9th St.
1937. Van Loon, Emily Lois, 1930 Chestnut St.
1933. Vastine, Jacob H., 2nd, 136 S. 16th St.
1947. Vastine, Mary F., Woman's Medical College of Pa.

1912. Vaux, Norris Wistar, 807 Spruce St.
1940. Voegelin, Adrian W., Germantown Professional Bldg.
1941. Vogel, Stoughton R., 246 Walnut Lane.
1903. Wadsworth, William S., 3914 Baltimore Ave.
1927. Wagers, Arthur J., 1429 Spruce St.
1928. Wagoner, George W., Haverford Gables, Haverford, Pa.
1938. Waldman, Joseph, 216 E. Gorgas Lane.
1906. Walker, John K., 139 Little Lane, Haverford, Pa.
1907. Walker, Warren, 136 S. 16th St.
1932. Walkling, Adolph A., 136 S. 16th St.
1895. Watson, Arthur W., 2013 Locust St.
1932. Watt, Charles C., Jr., 100 W. Coulter St.
1933. Waygood, James Jamison, 3464 School Lane.
1941. Weaver, Ruth H., 2601 Parkway.
1930. Weeder, S. Dana, 250 W. Tulpehocken St.
1920. Weidman, Fred D., 20 Tenby Rd., Havertown, Pa.
1933. Weiss, Benjamin P., The Lenox, 13th and Spruce Sts.
1923. Weiss, Edward, 269 S. 19th St.
1935. Whelan, G. L., 2100 Walnut St.
1921. Whitaker, William, 6771 Germantown Ave.
1936. White, Ellen Pawling Corson-, 1820 Pine St.
1925. Widmann, Bernard P., 250 S. 18th St.
1936. Wilder, Theodore S., Germantown Professional Bldg., Greene and Coulter Sts.
1914. Willard, De Forest P., 1726 Spruce St.
1935. Willard, John Harrington, 334 S. 15th St.
1939. Willauer, George, 6129 Greene St.
1907. Williams, Carl, School Lane and Greene St.
1924. Williams, Horace James, 5908 Greene St.
1937. Williams, John C., 6370 Germantown Ave.
1920. Williams, Philip F., 2206 Locust St.
1927. Williamson, Ernest G., 6353 Woodbine Ave.
1921. Wilson, George, 133 S. 36th St.
1945. Wilson, John F., 1930 Chestnut St.
1942. Wilson, Lucius R., 1305 Morris Road, Wynnewood, Pa.
1937. Wilson, Ross B., 1820 S. Rittenhouse Sq.
1902. Wilson, Samuel M., 1930 Chestnut St.
1940. *Winchell, A. Vaughn.
1941. Wirts, C. Wilmer, 2017 Delancey Pl.
1904. Wister, James W., 5430 Germantown Ave.
1933. Wohl, Michael G., 1727 Pine St.
1944. Wolf, Lewis R., 3474 Frankford Ave.
1918. Wolferth, Charles C., S.E. Cor. 36th & Spruce Sts.
1942. Wolman, Irving J., Lakeside Apts.
1893. Wood, Alfred C., 2035 Walnut St.
1932. Wood, Francis C., 212 Laurel Lane, Haverford, Pa.
1900. Wood, George B., N.E. Corner 20h and Chestnut Sts.
1903. Wood, Horatio C., 319 S. 41st St.
1944. Wood, H. Curtis, Jr., Skippack Pk., Whitemarsh, Pa.
1947. Wood, Oscar T., 2029 Delancey Pl.
1897. Woodward, George, W. Willow Grove Ave.
1928. Wright, Carroll S., 1402 Spruce St.
1937. Yaskin, Joseph C., 1832 Spruce St.
1943. Yawger, Nathaniel S., 1524 Chestnut St.

* On active service.

1941. Young, Barton R., Temple University Hosp.
1946. Zeigerman, Joseph H., 1836 Delancey St.
1894. Zentmayer, William, 1930 Chestnut St.
1947. Zintel, Harold A., Univ. of Pa. Hospital.
1933. Zulick, J. Donald, Abington Memorial Hospital, Abington, Pa.

Non-Resident Fellows

ELECTED

1941. Aronson, Roland S., Tilton General Hospital, Fort Dix, N. J.
1934. Bank, Joseph, Phoenix, Arizona.
1903. Biggs, M. H., Rutherfordton, N. C.
1937. Braceland, Francis, J., % Mayo Clinic, 102–11 Second Ave., S.W., Rochester, Minn.
1919. Brown, Henry P., Jr., Hueitien Hospital, Kunming, Yunnan, China.
1908. Cadbury, William W., Lingnan University, Canton, China.
1936. Camero, Anthony R., 657 S. Westlake Ave., Los Angeles, Cal.
1936. Clarke, Francis Mann, 116 New St., New Brunswick, N. J.
1930. Cottrell, James E., Memphis, Tennessee.
1942. Craighill, Margaret D., Topeka, Kansas.
1941. Dixon, Harold M., 3456 Newark St. N. W., Washington, D. C.
1897. Dorland, W. A. Newman, 447 Roslyn Pl., Chicago, Ill.
1905. Evans, Joseph S., Jr., 1300 University Ave., Madison, Wis.
1940. Forrester, James S., Harrisburg, Pa.
1933. Fowler, Kenneth, 2535 Horton Ave., San Diego, Cal.
1913. Gates, Nathaniel, 10 Peterboro, Detroit, Mich.
1931. Gilman, Robert Louis, Cheyney, Pa.
1936. Guthrie, Donald, 118 S. Wilbur Ave., Sayre, Pa.
1902. Gwyn, Norman B., 109 Madison Ave., Toronto, Canada.
1936. Hatch, Lerleen Clement, 245 Melbourne Ave., Akron, Ohio.
1928. Hayman, Joseph Marchant, Jr., Lakeside Hosp., 2065 Adelbert Rd., Cleveland, Ohio.
1892. Hinsdale, Guy, 1401 Rugby Rd., Charlottesville, Va.
1933. Hitzrot, Lewis H., Medical Director, Mercersburg Academy, Mercersburg, Pa.
1936. Hughes, Brady A., 5005 42d Place, North, Birmingham, Ala.
1899. Jopson, John H., Pawley's Island, S. C.
1902. Jump, Henry Draper, Seaside Park, N. J.
1947. Kelchner, Clyde H., 1125 Turner St., Allentown, Pa.
1931. Kinney, Willard H., 7300 Atlantic Ave., Ventnor, N. J.
1942. Kneedler, William H., 1821 Beverly Drive, Charlotte, N. C.
1941. Lockwood, John S., Columbia Presbyterian Medical Center, New York, N. Y.
1935. McGuire, Hunter H., 105 N. Braddock St., Winchester, Va.
1900. McReynolds, Robert Phillips, 213 S. Broadway, Los Angeles, Cal.
1935. Mason, James B., 4677 So. 34 St., Arlington, Va.
1932. Meade, Richard H., Jr., Chicago, Illinois.
1936. Middleton, William Shainline, 2114 Adams St., Madison, Wisconsin.
1937. Nicholson, Samuel T., 2d, The Hill School, Pottstown, Pa.
1905. Norris, George W., Dimock, Pa.
1926. Paul, John Rodman, Dept. Internal Medicine, Yale University, New Haven, Conn.
1907. Price, George E., Stimson Bldg., Seattle, Wash.
1936. Reisinger, John A., 901 20th St., N.W., Washington, D. C.
1907. Royer, B. Franklin, The Hall, R.D. 7, Chambersburg, Pa.
1945. Schell, James F., Veterans Hospital, New Castle, Del.
1913. de Schweinitz, George L., 85 E. Broad St., Bethlehem, Pa.
1941. Shands, Alfred R., Jr., Alfred I. duPont Institute, Rockland Rd., Wilmington, Del.
1932. Siegel, Alvin Erdreich, Medical Arts Building, Macon, Ga.

1934. Stewart, Sloan G., Pacific and North Carolina Avenues, Atlantic City, N. J.
1931. Stiles, Merritt H., Spokane, Washington.
1900. Swan, John M., 457 Park Ave., Rochester, N. Y.
1941. Tompkins, Pendleton, San Francisco, California.
1913. Vail, William Penn, Blairstown, N. J.
1897. Veasey, Clarence Archiblad, 1569 Paulsen Medical and Dental Bldg., Spokane, Washington.
1931. Walker, Herschel Carey, 320 Park Ave., New York City, N. Y.
1903. Weber, Charles H., 3 Arch Bay, Laguna Beach, California.

Honorary Fellows

Limited to Fifty, of Whom Twenty May be Foreigners

American

elected

1947. Longcope, Warfield Theobald, Johns Hopkins Hospital, Baltimore, Md.
1917. Miner, Charles Howard, B.S., M.D., Member of Board of Directors, Wilkes-Barre General Hospital; Board of Health, Wilkes-Barre; Board of Directors, White Haven Sanitarium Association and Penna. Tuberculosis Society. 264 S. Franklin St., Wilkes-Barre, Pa.
1947. Minot, George Richards, Thorndike Memorial Hospital, Boston City Hospital, Boston, Mass.
1936. Richards, Alfred Newton, PH.D., SC.D., M.D. (HON.), L.L.D., Professor of Pharmacology, School of Medicine, Vice-president in charge of Medical Affairs, Univ. of Pa. School of Medicine, Univ. of Pa., Phila.
1942. Russell, Frederick Fuller, M.D., Brig. Gen. Med. Corps, U. S. A. (Ret.). 54 Calburne Crescent, Brookline, 46, Mass.
1947. Stone, Robert Spencer, Univ. of California Medical School, San Francisco, Calif.

Foreign

1937. Dale, Sir Henry Hallett, C.B.E., F.R.S., M.A., M.D., F.R.C.P., Director, National Institute for Medical Research. The Wellcome Trustees, Dilke House, Mallet St., London, W. C. England.
1924. Hopkins, Sir F. Gowland, M.D., Biochemical Department, University of Cambridge, Cambridge, England.
1922. McCarrison, Sir Robert, K.T., C.I.E., M.D., D.SC., LL.D., F.R.C.P., Major-General, Indian Medical Service (retired). 18 Linton Rd., Oxford, England.

Honorary Associates

1942. Conklin, Professor Edwin G., Princeton University, Princeton, N. J.
1942. Donner, William Henry, Lincoln-Liberty Bldg., Philadelphia, Pa.

Necrological List

Resident Fellows	*Date of Election*	*Date of Death*
David J. Boon	May 7, 1924	February 11, 1947
Samuel Bradbury	May 6, 1929	August 30, 1947
Warren B. Davis	November 1, 1916	July 7, 1947
Irving W. Hollingshead	January 9, 1933	April 23, 1947
Walter I. Lillie	January 6, 1936	February 21, 1947
George P. Muller	January 4, 1905	February 18, 1947
P. S. Pelouze	October 4, 1922	March 12, 1947
William Pepper	November 5, 1902	December 3, 1947
William T. Sharpless	November 3, 1897	October 19, 1947
Non-resident Fellow		
John H. Musser, Jr.	October 6, 1915	September 6, 1947

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of the

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